SCIENTIFIC INTEGRITY AND FEDERAL POLICIES AND MANDATES: CASE STUDY 3—EPA'S DIOXIN REASSESSMENT

HEARING

BEFORE THE

SUBCOMMITTEE ON ENERGY AND ENVIRONMENT

OF THE

COMMITTEE ON SCIENCE

U.S. HOUSE OF REPRESENTATIVES

ONE HUNDRED FOURTH CONGRESS

FIRST SESSION

DECEMBER 13, 1995

[No. 39]

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*Ranking Minority Member
**Vice Chairman

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SCIENTIFIC INTEGRITY AND FEDERAL POLICIES AND MANDATES: CASE STUDY 3—EPA'S DIOXIN REASSESSMENT

WEDNESDAY, DECEMBER 13, 1995

U.S. HOUSE OF REPRESENTATIVES,
COMMITTEE ON SCIENCE,
SUBCOMMITTEE ON ENERGY AND ENVIRONMENT,
Washington, DC.

The subcommittee met at 10:15 a.m. in Room 2318 of the Rayburn House Office Building, the Honorable Dana Roharabacher, Chairman of the Subcommittee, presiding.

Mr. ROHRABACHER. This hearing of the Energy and Environment Subcommittee will come to order.

Let me begin by apologizing that we are late today. There are certain events in the world that sometimes take precedence over daily business.

One of the things that will take precedence over daily business is the deployment of American troops in great numbers to an area of conflict, and the Republican Party, which now dominates the House of Representatives, now the majority party, is trying to determine its policy as to what we will do in terms of the deployment of 20,000 American ground troops to Bosnia.

Obviously, this chairman and the other Republican members felt that letting this hearing start 45 minutes late was the thing to do rather than not to debate the issue of this troop deployment to the degree it was required.

We finished that vote, and we had a vote in the conference to decide the Republican position, and just for those who are interested, it was an overwhelming vote favoring the opposition to sending those troops to the Balkans, an opposition which would be substantial rather than just posturing and would be opposing the spending of any funds, Federal funds, in order to send American troops to the Balkans.

Whereas I was participating in that debate and felt strongly about it, that is why we are late.

I apologize, but that was the circumstance, and I hope you will understand.

This is a third in a series, and I apologize to my members as well, and this will not happen again and this was, I thought, a monumental issue that deserved my attention.

So I apologize. I am sorry.

Okay. This is the third in a series of hearings on how science is being used in Federal agencies to formulate policies and mandates. Today we will look at the EPA's dioxin reassessment.

Scientists have struggled to quantify the effects of dioxin compounds for over 20 years. It is particularly difficult because dioxin is a generic name given to 210 different compounds. Dioxin can only be produced by the high-temperature combustion of certain elements.

The EPA's reassessment began in 1991, after questions were raised about the scientific foundation for certain regulations.

A draft document was not produced until 1994, which was submitted to the EPA's Science Advisory Board. As a result, the board's recommendations, and that is of the board's recommendations, parts of the report will be revised, which the EPA says may take another year, lengthening the reassessment process to five years.

There is no question good science was produced in the EPA's document.

The EPA issued an open call to the best scientists in the field to participate, and many of them did. In many respects, the early stages of this process were a model of peer review and sound science, and the EPA is to be commended for it.

As a matter of fact, that is what the Republicans have been calling for. And yet this happened on its own, and we do commend them for it.

But when it came time to write the critical portion of the health effects of the document, it appears that the doors were closed and the EPA drew its own conclusions.

Of course, it is the end product that gets the attention and is used as the foundation for future regulations.

In a remarkable letter to Science magazine a year ago, 18 of the scientists who worked on the early portions of this reassessment said the EPA's conclusions are, and I quote, "are heavily dependent on many unproved assumptions and untested hypotheses."

They went on to urge, they went on to urge, "urge EPA to clearly distinguish regulatory policy from matters of scientific fact."

It is remarkable because most scientists, this is remarkable because most scientists are loath to air their concerns in public.

A number of the signatories, in fact, turned down an invitation to testify today, telling this committee they did not want to participate in the "political process," and that it could affect their work with the EPA.

It is clear these scientists feel strongly about the validity of the reassessment process used by the EPA.

There are no easy answers to the health questions raised by dioxin, and we are not here to imply that there are easy answers.

Instead we will take a look at how the EPA distinguishes regulatory policy from scientific fact, using the reassessment as a case in study.

To do that, we have a panel of scientists with differing views who are highly qualified on the topic.

Again, we have, this is the way I like to do things, instead of having just one side present their case and then perhaps having somebody down, you know, as the last witness whom nobody hears

presenting another case, we have tried to put people on both sides of this issue on the same panel so we can have an honest discussion.

Dr. William Farland directs the office of health and environmental assessment at the EPA and was charged with coordinating the reassessment.

Dr. Michael Gough served as a Federal expert consultant to the EPA's Science Advisory Board's health effects panel and has 15 years of experience at the Office of Technology Assessment in dioxin research.

Dr. George Lucier is director of the environmental toxicology program at the National Institute of Environmental Health Sciences and also contributed to the reassessment document.

Dr. Kay Jones is president of Zephyr Consulting and has worked on stationary and mobile-source combustion issues at the EPA, the Council on Environmental Quality, the World Health Organization, and Drexel University.

Later we will hear from Admiral Elmo Zumwalt, who, as chairman of the Agent Orange Coordinating Council, who has very strong feelings about the health effects of dioxin.

[The opening statement of Chairman Rohrabacher follows:]

OPENING STATEMENT
REP. DANA ROHRABACHER
EPA'S DIOXIN REASSESSMENT
DECEMBER 13, 1995

This is the third in a series of hearings on how science is being used in Federal agencies to formulate policies and mandates. Today we will look at EPA's Dioxin Reassessment.

Scientists have struggled to quantify the effects of dioxin compounds for over 20 years. It is particularly difficult because dioxin is a generic name given to 210 different compounds. Dioxin can only be produced by the high temperature combustion of certain elements.

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The EPA issued an open call to the best scientists in the field to participate and many of them did. In many respects, the early stages of this process were a model of peer review and sound science and the EPA is to be commended for it.

When it came time to write the critical portion of the Health Effects document, however, it appears the doors were closed and the EPA drew its own conclusions.

Of course, it is the end product that gets the attention and is used as the foundation for future regulations.

In a remarkable letter to Science Magazine one year ago, 18 of the scientists who worked on early portions of this reassessment said the EPA's conclusions "are heavily dependent on many unproved assumptions and untested hypotheses."

They went on to "urge EPA to clearly distinguish regulatory policy from matters of scientific fact."

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It is remarkable because most scientists are loathe to air their concerns in public. A number of the signatories turned down an invitation to testify today, telling this committee they did not want to participate in the "political process" and that it could affect their work with EPA.

It's clear these scientists feel strongly about the validity of the reassessment process used by the EPA.

There are no easy answers to the health questions raised by dioxin, and we are not here to imply there are.

Instead, we will take a look at how the EPA distinguishes regulatory policy from scientific fact, using the reassessment as a case study.

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Later we will hear from Admiral Elmo Zumwalt, Chairman of the Agent Orange Coordinating Council, who has strong feelings about the health effects of dioxin.

# # #

Mr. ROHRABACHER. Before we turn to our first panel, I will ask our distinguished, I guess it is acting ranking minority member, Mr. Roemer, for an opening statement.

Mr. ROEMER. Thank you, Mr. Chairman. I appreciate being recognized, and thank you for having this hearing this morning.

As you know, I am a strong supporter of risk assessment as an important tool to help agencies craft reasonable, cost-effective regulations.

I think it is very appropriate for the Subcommittee to review the risk assessment practices of the Federal agencies so that we can better understand the promises and limitations of risk assessment, the opportunities to improve it, and the potential impacts of pending risk assessment and regulatory reform legislation.

The dioxin risk assessment is probably the most expensive, complex, and scientifically challenging risk assessment ever undertaken by the EPA.

EPA deserves being commended for undertaking this reevaluation of the science and for making such unprecedented efforts to open the process up for public participation and scientific peer review.

It is, however, a very complicated model. Some modifications and suggested improvements for EPA are in order, and we hope to hear those today. Some mistakes have been made in the process. Even a cursory review of the testimony shows that the science underlying the assessment is very complicated and subject to dispute even among respected experts.

Significant scientific uncertainties remain.

Given the potentially enormous costs associated with further EPA dioxin regulations, it shouldn't be all that surprising that various interest groups have been busy spinning the EPA risk assessment and the Science Advisory Board review of EPA's works.

Faced with scientific disputes, we can't act as a science court. Ultimately, we have to leave the resolution of scientific issues to the scientific process.

The question is whether that process has been fair and whether the risk assessment fairly represents the science on which it has been based.

In putting together its risk assessment chapter, EPA initially consulted with outside experts to identify the key risk assessment and risk characterization issues.

It then worked, together with experts from other Federal regulatory agencies, to draft the risk assessment chapter.

In September 1994 EPA published a public review draft of the risk assessment and not only asked for public comments but also held five public hearings across the country to obtain those comments.

EPA submitted the draft report and the extensive public comments it received to EPA's scientific advisory board for an independent scientific peer review.

A special 39-member SAB panel, representing a variety of disciplines and viewpoints, was appointed, met, and issued a report. EPA is now in the process of rewriting its assessment to meet the concerns expressed by the SAB.

While EPA's process could probably be improved, I look forward to hearing suggestions in the testimony for such specific improvements.

It certainly appears that the process was open for full public participation, debate, and scientific peer review.

As far as I can tell, the process seems to be working. It seems somewhat premature to judge EPA's efforts until the final product is complete.

I am also interested to know what effect the passage of a bill like H.R. 1022 would have on future risk assessments, taking the dioxin risk experience into account.

The dioxin risk assessment has already taken over four years, involved hundreds of scientists, generated mountains of reports, and cost the taxpayers a lot of good money.

I am particularly concerned that, without a provision like the amendment I offered on the Floor to prevent expansive, new judicial review of risk assessments, we wouldn't even be this far along.

Instead, the environmental groups or the industry groups would have hauled EPA into court, where lawyers and judges instead of scientists would be trying to resolve some of these scientific disputes.

Mr. Chairman, I would ask unanimous consent that a statement to the Committee from the EPA Science Advisory Board be made part of the record, and, Mr. Chairman, if there is any remaining time on our side, I would like to yield to the gentleman, our former chairman, Mr. Brown.

Mr. ROHRABACHER. Your letter will be, without objection, will be made part of the record.

[The prepared statement of Congressman Roemer follows:]

Statement of the Hon. Tim Roemer
Hearing on EPA Dioxin Reassessment
Energy and Environment Subcommittee

December 13, 1995

Thank you, Mr. Chairman. As you know, I am a strong supporter of risk assessment as an important tool to help agencies craft reasonable and cost-effective regulations. I think it is very appropriate for the Subcommittee to review the risk assessment practices of the federal agencies so that we can gain a better understanding of the promises and limitations of risk assessment, the opportunities to improve it, and the potential impacts of pending risk assessment and regulatory reform legislation.

The dioxin risk assessment is probably the most expensive, complex and scientifically-challenging risk assessment ever undertaken by the EPA. EPA deserves commendation for undertaking this reevaluation of the science and for making such unprecedented efforts to open the process up for public participation and scientific peer review.

Even a cursory review of the testimony shows that the science underlying the assessment is very complex and subject to dispute even among respected experts. Significant scientific uncertainties remain. Given the potentially enormous costs associated with further EPA dioxin regulations, it shouldn't be all that surprising that various interest groups have been busy "spinning" the EPA risk assessment and the Science Advisory Board review of EPA's work.

For the most part, we are not scientists on this Subcommittee. Faced with scientific disputes, we can't act as a "science court." Ultimately, we have to leave the resolution of scientific issues to the scientific process. The question is whether that process has been fair and whether the risk assessment fairly represents the science on which it is based.

In putting together its risk assessment chapter, EPA initially consulted with outside experts to identify the key risk assessment and risk characterization issues. It then worked together with experts from other federal regulatory agencies to draft the risk assessment chapter. In September, 1994, EPA published a public review draft of the risk assessment and not only asked for public comments, but also held five public hearings across the country to obtain comments.

EPA submitted the draft report and the extensive public comments it received to EPA's Scientific Advisory Board for an independent scientific peer review. A special 39-member SAB panel representing a variety of disciplines and viewpoints was appointed, met, and issued a report. EPA is now in the process of rewriting its assessment to meet the concerns expressed by the SAB.

While EPA's process could probably be improved -- and I look forward to hearing suggestions in the testimony for such improvements -- it certainly appears that the process was open for full public participation, debate, and scientific peer review. As far as I can tell, the process seems to be working. It seems somewhat premature to judge EPA's efforts until the final work product is complete.

I also am interested to know what effect the passage of a bill like H.R. 1022 would have on future risk assessments, taking the dioxin risk experience into account. The dioxin risk assessment has already taken over 4 years, involved hundreds of scientists, generated mountains of reports, and cost the taxpayers a lot of good money. I am particularly concerned that without a provision like the amendment I offered on the floor to prevent expansive new judicial review of risk assessments, we wouldn't even be this far along. Instead, the environmental groups or the industry groups would have hauled EPA into court where lawyers and judges instead of scientists would be trying to resolve some of these scientific disputes.

Thank you, Mr. Chairman, and I would yield any remaining time to the ranking member of the full Committee, Mr. Brown.

Mr. ROHRABACHER. We very happily would like to hear from former distinguished chairman, Mr. Brown of California.

Mr. BROWN. Mr. Chairman, I compliment you on scheduling this risk assessment hearing. This is an invaluable part of both maintaining oversight over a complex subject and providing an opportunity for members to become familiar with a debate which I have been participating in for 15 years and still don't fully understand. And our members are going to need all the help they can get in mastering this.

I want to merely raise one point, Mr. Chairman, which I hope is not construed as being overly critical. In the charter for this hearing it was indicated that we would have a witness from the Science Advisory Board.

We have a letter from the Science Advisory Board signed by its executive director indicating they would like to provide a witness if the committee desires.

And yet we do not have a witness from the Science Advisory Board on the panel.

We have a very good substitute in the form of Dr. Gough, but I think he would be the first to admit he is not a member of the Science Advisory Board.

Mr. ROHRABACHER. Thank you, Mr. Brown. I would just like to let you know Morton Lipman, Dr. Morton Lipman, the chairman of the health effects panel, was the first person that was invited to testify.

He was unable to attend. We have done our utmost to get the most qualified people on both sides of the argument to be on the panel.

I mean, this is something we strove to do. Strove, is that the right word? Strove? Strived? We strove.

No, we didn't strove, we strived.

Mr. BROWN. Mr. Chairman, I am not criticizing the makeup of the panel. I think you do have a balanced panel.

Mr. ROHRABACHER. All right.

Mr. BROWN. But I was merely pointing out that we could have asked for another member of the panel, and they have offered to provide such a member.

But I am sure that this will not damage the value of this hearing substantially.

Mr. ROHRABACHER. Thank you very much.

Now I guess we have Mr. Doyle, who would like to have an opening statement. Certainly.

Mr. DOYLE. Thank you, Mr. Chairman.

I want to thank you for calling today's hearing, and I don't want to take up a lot of the subcommittee's time, but there are a couple points I feel compelled to make before we begin.

First, I want to commend those in industry who have put forth great effort to minimize dioxin use.

In particular, the record of the pulp and paper industry is especially commendable.

I am hopeful that Congress will in some way move to address the regulatory issues which seem to be based on a particular outcome of the ongoing research on dioxin.

While I think we need to honestly examine how EPA is conducting this research, we must also not presuppose its outcome.

Secondly, as the only member of the Science Committee who also serves on the Veterans' Affairs Committee, I can tell you that there are very few times that an issue of interest to both committees.

However, the subject of today's hearing is one of those occasions.

The issue of dioxin is of special importance to our Nation's veterans, due, in large part, to the controversy surrounding the effects of Agent Orange exposure during the Vietnam War.

This is widely known by all Members of Congress. So I was somewhat surprised that the veterans community had no voice in the initial list for this hearing.

I would like to thank Chairman Rohrabacher for recognizing this omission and inviting Admiral Zumwalt to be with us here today.

I have also taken the liberty of contacting Dr. Paul Sutton of the Vietnam Veterans of America about today's hearing, and I would like to ask unanimous consent to include in the record our correspondence, as well as a statement on behalf of VVA.

Thank you, Mr. Chairman, and I yield back my time.

Mr. ROHRABACHER. Without objection, that correspondence will be included in the record.

[The prepared statement of Congressman Doyle follows:]

OPENING STATEMENT OF REP. MIKE DOYLE
SUBCOMMITTEE ON ENERGY & ENVIRONMENT
HEARING ON EPA'S DIOXIN REASSESSMENT
December 13,1995

Mr. Chairman, I want to thank you for calling today's hearing.

I don't want to take up a lot of the Subcommittee's time, but there a couple points I feel compelled to make before we begin.

First, I want to commend those in industry who have put forth great effort to minimize dioxin use. In particular, the record of the pulp and paper industry is especially commendable. I am hopeful Congress will, in some way, move to address the regulatory issues which seem to be based on a particular outcome of the ongoing research on dioxin. While I think we need to honestly examine how EPA is conducting this research, we must also not presuppose its outcome.

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The issue of dioxin is of special importance to our nation's veterans, due in large part to controversy surrounding the effects of Agent Orange exposure during the Vietnam War. This is widely known by all Members of Congress, so I was somewhat surprised that veterans' community had no voice in the initial witness list for this hearing. I would like to thank Chairman Rohrbacher for recognizing this omission and inviting Admiral Zumwalt to be here with us today.

I also have taken the liberty of contacting Dr. Paul Sutton of the Vietnam Veterans of America about today's hearing. I would like to ask unanimous consent to include in the record our correspondence as well as his statement on behalf of VVA.
Again, thank you Mr. Chairman, and yield back my time.

Mr. ROHRABACHER. This hearing is supposed to be focused on the process, the reassessment process, and that is our authority.

That's what this committee has authority over, our subcommittee has committee authority over. And we do not, we are not trying to determine the toxicity or lack of toxicity of dioxin.

And because we felt that your request was, you know, heartfelt and thought out but not necessarily under the jurisdiction of the committee but we went ahead with your request, and that's why Admiral Zumwalt will be testifying today, as a courtesy to those who feel so strongly on this issue.

However, let me repeat, our jurisdiction is simply over the reassessment process, and we are not here to determine dioxin itself, whether or not that is a toxic material or not.

So, with that, I think we should proceed with our first witness, and again I will apologize to our witnesses for being late, and some of my other Republican colleagues, who are probably still participating in that conference, will be joining us shortly.

Mr. ROHRABACHER. Dr. Farland.

STATEMENTS OF WILLIAM H. FARLAND, PH.D., DIRECTOR, NATIONAL CENTER FOR ENVIRONMENTAL ASSESSMENT, OFFICE OF RESEARCH AND DEVELOPMENT, U.S. ENVIRONMENTAL PROTECTION AGENCY, ACCOMPANIED BY LINDA BIRNBAUM, DIRECTOR, DIVISION OF EXPERIMENTAL TOXICOLOGY, NATIONAL HEALTH AND ENVIRONMENTAL EFFECTS LABORATORY

Dr. FARLAND. Good morning. I am Dr. William Farland, the Director of the National Center for Environmental Assessment within the Office of Research and Development at the U.S. EPA.

I am accompanied here today by Dr. Linda Birnbaum, the Director of the Division of Experimental Toxicology at our National Health and Environmental Effects Laboratory and EPA's chief research scientist on dioxin and related compounds.

Linda is also an internationally recognized expert on the topic.

Mr. Chairman, as you mentioned, I have the agency lead on the current dioxin reassessment project, and I have worked on evaluating the risks of dioxin and related compounds since the early 1980s.

I, along with Dr. James Witlock, the Chair of the Department of Molecular Pharmacology at Stanford, was responsible for the mechanisms of action chapter in the health reassessment.

In addition, I was the principal author of the risk characterization chapter, along with Dr. Birnbaum, my colleagues from EPA, from several agencies of the Department of Health and Human Services and from the U.S. Department of Agriculture and several scientists from academic institutions.

As you no doubt know by now, scientists from the U.S. Environmental Protection Agency, other Federal agencies, and the general scientific community have been involved in a comprehensive scientific reassessment of dioxin-related compounds since 1991.

Two thousand pages of external review documents, drafts, were made available in September 1994 by the agency for public comment and review by the EPA's Science Advisory Board.

This process has been a model for open participatory environmental health assessment. Peer review has been an integral part of the entire reassessment process.

Extensive comments have been received and will be the basis for revisions to the draft documents.

These documents and subsequent comments highlight a number of issues which are of broad scientific interest.

Now, in answer to the questions that were posed on page 2 of the hearing charter, I have discussed these in my written testimony, but, in brief, the EPA believes that the risk characterization was consistent with the scientific findings contained in the earlier chapters; secondly, that contrary to the implication of the charter, the question, the risk characterization was informed by input from a panel of external reviewers of the draft chapters, drafted by Federal scientists, and it was peer reviewed. It, like the rest of the report, involved both EPA and non-EPA drafters and reviewers.

EPA's risk characterization does not rely solely on high levels of exposure to animals, but integrates animal data with limited human information.

Animal data have been obtained at levels of exposure that are comparable to human exposures. The human information has been obtained on populations exposed at background levels and above.

Finally, while the regulatory impacts assessments are carried out on every regulation that might be issued, no analysis of potential economic impacts on regulations that may be based on this reassessment will be conducted until the reassessment is complete and a comprehensive agencywide strategy has been developed.

As you mentioned, dioxin is the term used for a group of chemical compounds with similar chemical structure, which are inadvertently created through a number of activities, including combustion, certain types of chemical manufacture, chlorine bleaching of pulp and paper, and other industrial processes.

They are produced in very small quantities compared to other pollutants; we estimate less than 30 pounds of toxic equivalents annually in the U.S.

However, because they are highly toxic, they have been treated as significant environmental pollutants since the early 1970s.

In 1985 EPA published a scientific review of the health effects of 2,3,7,8-TCDD, the most toxic of the dioxin compounds. That assessment has served as the scientific basis for dioxin risk estimates for all U.S. EPA programs.

In 1991 the EPA announced that it would conduct a comprehensive scientific reassessment of the health risks of exposure to the family of compounds generally known as dioxin.

EPA has undertaken this task in light of significant advances in scientific understanding of the mechanisms of dioxin toxicity, significant new studies of dioxin's carcinogenic potential in humans, and increased evidence of other adverse effects.

The reassessment is part of the agency's goal to improve its research and science base and to incorporate this knowledge into EPA decisions.

The reassessment consists of two documents, each of about a thousand pages long and each published in several volumes.

One of these documents addresses the human health effects of dioxin. The second focuses on sources and levels of exposure.

The reassessment is a scientific document and does not address regulatory policy or issues.

Volume 3 of the health effects document is the risk characterization chapter. This chapter integrates the findings of both the effects and exposure documents, outlines important inferences and science policy assumptions made in the absence of complete information, and describes potential hazards and risks posed by dioxin.

The draft study not only updates the '85 document but also represents an ongoing process to build a scientific consensus regarding the question of dioxin's potential to produce toxic effects.

To help foster this consensus, EPA has worked to make each phase of the dioxin reassessment an open and participatory one.

These efforts have included the involvement of outside scientists as principal authors of chapters, numerous public meetings to take comments on our plans and progress, publication of earlier drafts of our public work for public comment and review.

The current external review draft has been made available for public comment and full scientific review. Results of this review, which took place from September 1994 to October 1995, will be used to revise and update the drafts over the next year.

When this process is completed, we anticipate having an up-to-date and thorough scientific evaluation of dioxin that is on the cutting edge of environmental toxicology and exposure assessment.

My written testimony has extensive details about the findings and issues contained in the draft Health Assessment of Dioxin and Related Compounds.

Regarding health risks, the draft study affirms the association of dioxin and cancer. In its 1985 assessment, EPA concluded that dioxin is a proven animal carcinogen and a probable human carcinogen under some conditions of exposure.

The current draft reaches the same conclusions but with greater confidence because of additional published human data and enhanced understanding of dioxin's mode of action.

The SAB agreed with these conclusions. Based upon both animal and human evidence, EPA's estimate of dioxin cancer potency is essentially unchanged from that of 1985.

The draft reassessment differs significantly from the 1985 document in its evaluation of dioxin's noncancer effects.

Today we have a stronger body of evidence to suggest that, at some dose, dioxin exposures can result in a number of effects in humans and some of these effects may even have an adverse impact on health.

These effects may include developmental and reproductive effects, immune suppression and disruption of regulatory hormones.

We currently have limited direct evidence to show that any of these noncancer effects occur in humans at everyday levels of exposure. However, new studies are appearing which support earlier findings.

We can infer from the information on levels of dioxin and related compounds that persist and recycle in the environment and are found in minute quantities in food and in people that average ev-

eryday exposure levels are close to exposures that are known to cause such effects in laboratory animals.

Humans exposed to dioxin at several times average background levels in the general population have also shown indications of subtle effects which may or may not represent an adverse effect to health.

In addition, the exposure document provides the first comprehensive survey of U.S. sources of dioxin and related compounds.

A large variety of sources of dioxin have been identified, and others may exist. The available information suggests the presence of dioxin-like compounds in the environment has occurred primarily as a result of industrial practices and is likely to reflect changes in release over time.

The principal identified sources of environmental release may be grouped into four major types. combustion and incineration sources; chemical manufacturing and processing sources; industrial and municipal processes; and reservoir sources.

Although the current draft suggests that municipal and hospital waste incineration may account for the majority of the known releases, comments suggest the need to reevaluate these estimates based on changes in the number of active facilities and technologies applied to incineration in the past few years.

Additional complex issues associated with the assessment include the air-to-food-to-humans pathway of exposure, the concept of toxicity equivalence, background exposures, and dioxin's mode of action which make it similar to an environmental hormone.

Other issues, such as the meaning of subtle and perhaps adaptive rather than adverse effects of dioxins and the calculations of margins of exposure, have also been discussed in my written testimony.

The risk characterization, Chapter 9, for dioxin and related compounds was developed as an integrated analysis of information from the exposure document and from the eight health effects chapters.

Key assumptions were identified and discussed, and uncertainties attendant to the findings of the report were highlighted in the integrated analysis and the risk characterization summary.

Issues to be discussed in the risk characterization chapter emerge directly from the previous assessment work carried out by external authors as well as EPA scientists, were articulated by commenters on the process of the reassessment in numerous public meetings, and specifically came from recommendations made by peer panel reviewers of earlier versions of the reassessment chapters in 1992.

This process led to the development of a draft risk characterization, primarily by EPA authors but with the assistance of some outside scientists.

This early draft was reviewed extensively within the EPA and by numerous Federal agencies. The interagency review resulted in the formation of a drafting team from EPA, HHS, and USDA to address the comments of the reviewers.

An unauthorized and unintended release of the interagency review draft also produced a round of unsolicited external comments in June and July of 1994.

All of this input formed the basis for the external review draft of the risk characterization which was released in September of '94 for broad public comment.

Despite the question raised in the charter of this hearing, the risk characterization is consistent with the findings contained in the earlier chapters. Any minor inconsistencies identified by peer review will be rectified in the revised version of the document.

In its October 1995 report to the administrator, the SAB noted a number of strengths in the risk characterization.

First, "by focusing serious attention on the various noncancer effects, the agency has dispelled any misconception that EPA's risk assessment process is overly preoccupied with carcinogenic effects."

Second, "by evaluating an entire group of compound classes with a common attribute rather than a single compound, the agency responds to the generally mistaken criticism that its risk assessment process can only address issues on a chemical-by-chemical basis."

Third, "in the opinion of most committee members, a useful comparative perspective is provided in the draft conclusions where the agency highlights the fact that the margin of safety between the background exposures and the levels of exposure where effects have been seen in test animals for dioxin-like compounds is smaller than EPA usually sees from any other compounds."

On the other hand, the SAB noted three major weaknesses. First, the presentation, this is a quote, "The presentation portrayed in the draft conclusion is not balanced." This statement is footnoted with the following. "Several members of the committee do not agree with the statement and regard the EPA presentation and the inferences drawn as appropriately conservative within the context of public health protection."

Second, "Important uncertainties associated with the agency's conclusions are not fully recognized and subjected to feasible analyses."

Third, "The characterization of noncancer effects is not performed in a manner that allows meaningful analysis of the incremental benefits of risk management alternatives." This statement also was footnoted with the following statement. "A minority within the committee finds the noncancer risk characterization to be appropriate for use within a public health perspective.

However, they agree that the reassessment's characterization is not performed in a manner which will be very useful in the analysis of the incremental benefits of risk management by those who will be concerned with microlevel incremental costs."

These comments, with their specified examples as well as more specific comments on the other chapters, will be dealt with in the revision process.

EPA is now in the process of addressing the comments on the external review draft of the dioxin reassessment. Comments from the SAB will be considered along with those from the broader scientific community and the public.

Details of our proposed process for dealing with the comments is contained in my written testimony.

With regard to timing of these events, the revision process has already begun. Drafting of the chapter summaries and the revised

dose-response chapter and the risk characterization are anticipated to be complete by March 1996.

Peer panel meetings are expected to be held on these documents early in May, particularly on chapter 8, the dose-response chapter and chapter 9, the characterization chapter.

Documents will be referred to the SAB in June, with a review meeting to be held as soon as possible thereafter.

Final documents are targeted for printing in August, with release occurring in September 1996.

Obviously, this assumes that no major new issues arise during the revision process that would require extensive additional analysis or obviate the current approach for assessing dioxin risk.

While the science of the reassessment is undergoing further peer review, EPA will be examining the reassessment's policy implications to determine what changes, if any, are needed in existing programs.

While regulatory impact assessments are carried out on every regulation that might be issued, no estimates of the economic impact to the public from regulations that may be based on this reassessment have yet been carried out. Throughout the reassessment process, the agency has repeatedly stated that existing EPA efforts and programs will not be changed on the basis of this draft reassessment.

However, they may change significantly after the completion of the report.

EPA is committed to developing an agencywide strategy for managing dioxin risks concurrent with completion of the dioxin reassessment.

As with the reassessment, we want to provide an opportunity for public input into our policy evaluations.

I thank you for the time this morning, and I will be glad to take questions whenever it is appropriate.

Mr. ROHRABACHER. Yes.

Dr. Farland, we actually, the committee would like to have had a shorter presentation, but I let you go on because I think that what you are saying is basically the basis of what this discussion is supposed to be about.

So I was very happy to have you have a little longer time to present your case.

Dr. FARLAND. Thank you, Mr. Chairman.

[The prepared statement of Dr. Farland follows:]

Testimony of
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Director,
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Office of Research and Development
U.S. Environmental Protection Agency
before the
Energy and Environment Subcommittee
of the
Committee on Science,
House of Representatives

December 13, 1995

Introduction

Scientists from the U.S. Environmental Protection Agency (USEPA), other Federal agencies and the general scientific community have been involved in a comprehensive scientific reassessment of dioxin and related compounds since 1991. External review drafts of the reassessment documents entitled "Estimating Exposure to Dioxin and Related Compounds" and "Health Assessment of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and Related Compounds" were made available in September, 1994 by the Agency for public comment and review by the EPA's Science Advisory Board (SAB). This process has been a model for open, participatory environmental health assessment. Peer review has been an integral part of the entire reassessment process. Extensive comments have been received and will be the basis for revisions to the draft documents. These documents and subsequent comments highlight a number of issues which are of broad scientific interest. Answers to the questions posed on page 2 of the Hearing Charter are discussed in the text that follows. In brief, 1) the EPA believes that the risk characterization was consistent with the scientific findings contained in the earlier chapters; 2) contrary to the implication of the question, the risk characterization was informed by input from a panel of external reviewers of the draft chapters, drafted by Federal scientists and was peer reviewed. It, like the rest of the report, involved both EPA and non-EPA drafters and reviewers; 3) EPA's risk characterization does not rely solely on high levels of exposure to animals, but integrates animal data with limited human information. Animal data have been obtained at levels of exposure comparable to human exposures, and human information has been obtained on populations exposed at background levels and above; and 4) while regulatory impact assessments are carried out on every regulation that might be issued, no analysis of the potential economic impact on regulations that may be based on this reassessment will be conducted until the reassessment is complete and a comprehensive Agency-wide strategy has been developed.

Background

Dioxins are a group of chemical compounds inadvertently created through a number of activities including: combustion, certain types of chemical manufacture, chlorine bleaching of pulp and paper, and other industrial processes. Dioxin is produced in very small quantities compared to other pollutants (around 30 pounds TEQ[1] annually in the U.S.); however, because it is highly toxic, it has been treated as a significant environmental pollutant since the early 1970's. U.S. EPA first took action against dioxin as a contaminant of the herbicide 2,4,5-T in 1979. Since then, EPA has expanded its dioxin control efforts to each of its major programs.

In 1985 EPA published a scientific review of the health effects of 2,3,7,8-TCDD, the most toxic of the dioxin compounds. That assessment has served as the scientific basis for dioxin risk estimates for all U.S. EPA programs. In April 1991, EPA announced that it would conduct a comprehensive scientific reassessment of the health risks of exposure to the family of compounds generally known as dioxin (2,3,7,8-TCDD and other dioxin-like compounds, including certain dioxin-like polychlorinated biphenyls (PCBs)). EPA has undertaken this task in light of significant advances in our scientific understanding of mechanisms of dioxin toxicity, significant new studies of dioxin's carcinogenic potential in humans, and increased evidence of other adverse health effects. The reassessment is part of the Agency's goal to improve its research and science base and to incorporate this knowledge into EPA decisions. In September, 1994, EPA released a "public review draft" of its dioxin reassessment. This release marked a mid-point in EPA's effort to reevaluate the scientific understanding of dioxin. While the reassessment has been underway, EPA has continued to move forward in implementing its dioxin control programs, based on the 1985 assessment and, in most cases, applying technology-based rather than risk-based solutions. In the past fifteen years, EPA has taken action under every one of its major statutes to control the risks of dioxin. No regulatory action has been undertaken by the Agency based on the results of this draft reassessment. Throughout the reassessment process the Agency has repeatedly stated that existing EPA efforts and programs will not be changed on the basis of this draft reassessment, but they may change significantly after the completion of the report.

1TEQ = Toxic Equivalents. TEQ is an internationally recognized convention for expressing the toxicity of a complex mixture of multiple dioxin-like compounds, varying in their toxicity, as an equivalent amount of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), the reference compound for this class.

Science Reassessment

In September 1994, the EPA released the public review draft of the full reassessment. The reassessment consists of two documents, each about a thousand pages long, and each published in several volumes. One of these documents addresses the human health effects of dioxin; the second focuses on sources and levels of exposure. The reassessment is a scientific document and does not address regulatory policy or issues. An effort to address regulatory policy issues raised by the reassessment will be carried out in separate, public discussions in the winter and spring of 1996. Volume three of the health effects document is the Risk Characterization chapter . This chapter integrates the findings of both the effects and exposure documents, outlines important inferences and science policy assumptions made in the absence of complete information, and describes the potential hazards and risks posed by dioxin.

The draft study not only updates the 1985 document, but also represents an ongoing process to build a broad scientific consensus regarding the question of dioxin's potential to produce toxic effects . To help foster this consensus, EPA has worked to make each phase of the dioxin reassessment an open and participatory process. These efforts have included the involvement of outside scientists as principal authors of several chapters, numerous public meetings to take comment on our plans and progress, and publication of earlier drafts of our work for public comment and review. The current "external review" draft has been made available for public comment and full scientific review. Results of this review, which took place from September, 1994 to October, 1995, will be used to revise and update the drafts over the next year. When this process is completed, we anticipate having an up-to-date and thorough scientific evaluation of dioxin that is at the cutting edge of environmental toxicology and exposure assessment.

Regarding health risks, the draft study reaffirms the association of dioxin and cancer. In its 1985 assessment, EPA concluded that dioxin is a proven animal carcinogen and a probable human carcinogen. The current draft report reaches the same conclusion, but with greater confidence because of additional published human data and enhanced understanding of dioxin's mode of action. Based upon both animal and human evidence, EPA's estimate of dioxin's cancer potency is essentially unchanged from that of 1985.

The draft reassessment differs significantly from the 1985 document in its evaluation of dioxin's non-cancer effects. Today we have a stronger body of evidence to suggest that at some dose, dioxin exposure can result in a number of non-cancer effects in humans, and that some of these effects may have an adverse impact on health. These effects may include developmental and reproductive effects, immune suppression, and disruption of regulatory hormones. We currently have very limited

direct evidence to show that any of these non-cancer effects occur in humans at everyday levels of exposure. However, we can infer from the information on levels of dioxin and related compounds in the environment, in food, and in people that average everyday exposures are close to exposures that are known to cause such effects in laboratory animals. Humans exposed to dioxins at several times average background levels in the general population have also shown indications of subtle effects which may or may not represent an adverse impact on their health.

U.S. Exposure Survey

The Exposure Document provides the first comprehensive survey of U.S. sources of dioxin and related compounds. A large variety of sources of dioxin have been identified and others may exist. The available information suggests that the presence of dioxin-like compounds in the environment has occurred primarily as a result of industrial practices and is likely to reflect changes in release over time. The principal identified sources of environmental release may be grouped into four major types: combustion and incineration sources; chemical manufacturing/processing sources; industrial/municipal processes; and reservoir sources. Although the current draft suggests that municipal and hospital waste incineration may account for the majority of known releases, comments suggest the need to reduce these estimates based on changes in numbers of active facilities and technologies applied to incineration in the past few years. Also, additional sources have been identified and will be further addressed in future versions of the document.

Because dioxin-like chemicals are persistent and accumulate in biological tissues, particularly in animals, the scientific community has hypothesized since the late 1980's that the major route of human exposure is through ingestion of foods containing minute quantities of dioxin-like compounds. The EPA reassessment document adopts this hypothesis. This pathway results in wide-spread, low-level exposure of the general population to dioxin-like compounds. Certain segments of the population may be exposed to additional increments of exposure by being in proximity to point sources or because of dietary practices. The actual levels of dioxin and related compounds in the environment and in food in the U.S. are based on relatively few samples and must be considered quite uncertain. However, they seem consistent with levels measured in a number of studies in Western Europe and Canada. The consistency of these levels across industrialized countries provides reassurance that the U.S. estimates are reasonable. Collection of additional data to reduce uncertainty in U.S. estimates of dioxin-like compounds in the environment and in food represents an important data need. Data collection is currently underway in a series of studies being carried out by EPA and U.S.Department of Agriculture (USDA) scientists. Recent data on levels of dioxin-like compounds in the fat of beef suggests similar, if not slightly lower, levels compared to previous information. Additional food products are being collected and dioxin levels are being analyzed.

Air to Food Hypothesis

This assessment adopts the hypothesis that the primary mechanism by which dioxin-like compounds enter the terrestrial food chain is via atmospheric deposition. Dioxin and related compounds enter the atmosphere directly through air emissions or indirectly, for example, through volatilization from land or water or from re-suspension of particles. Deposition can occur directly onto soil or onto plant surfaces. At present, it is unclear whether atmospheric deposition represents primarily current contributions of dioxin and related compounds from all media reaching the atmosphere, or whether it is past emissions of dioxin and related compounds which persist and recycle in the environment. Understanding the relationship between these two scenarios will be particularly important in understanding the relative contributions of individual point sources of these compounds to the food chain and assessing the effectiveness of control strategies focussed on either current or past emissions of dioxins in attempting to reduce the levels in food. Commentors have also highlighted the importance of better understanding atmospheric transformation processes in order to adequately model fate and transport of these compounds from source to receptor (human or ecological).

Toxicity Equivalents

Because the assessment of dioxin and related compounds involves the evaluation of approximately eighteen major persistent chemicals and hundreds of others, often occurring as complex environmental mixtures, an approach has been developed to overcome the lack of information on individual members of this class. Throughout the reassessment, concentrations of dioxin and related compounds have been presented as TCDD equivalents (TEQs). TCDD is the best studied of this class of compounds and is the reference compound with regard to determination of toxicity equivalence factors (TEFs). Other dioxin-like compounds are assigned TEFs based on inspection of available physical, chemical and toxicologic information. Other approaches to evaluating the toxicity of dioxin-like compounds such as assuming that all are as toxic as 2,3,7,8-TCDD, or assuming that they do not contribute significantly to the toxicity of this family of compounds given 2,3,7,8-TCDD's potency are generally considered to be unacceptable. Therefore, the international scientific community, as represented by World Health Organization (WHO) and NATO scientific committees, the EPA and several states have adopted the TEF approach as a useful, albeit uncertain, procedure in the face of incomplete data on this family of compounds, and with the prospects of ever filling all of the data gaps improbable.

The strengths and weaknesses as well as the uncertainties associated with the TEF/TEQ approach have been discussed in detail in the documents but further attention will be needed to provide appropriate perspective on their use. In particular,

additional care will be given to delineating the contribution of TCDD, the best studied of these compounds, to estimated TEQ. The assessment of toxicity of dioxin and related compounds presents a difficult "complex mixture" problem. Use of the TEFs for dioxin-like PCBs in estimating total TEQ has received extensive comment. As noted, the use of the TEQ approach is fundamental to the evaluation of this group of compounds and as such represents a key assumption upon which many of the conclusions in this reassessment hinge. Additional data are being collected to evaluate this issue both in terms of the assignment of appropriate TEFs and in addressing issues such as additivity of the TEFs in environmental samples and food or in human blood, tissue, or mother's milk.

"Background" Exposure

The term "background" exposure has been used throughout this reassessment to describe exposure of the general population, who are not exposed to readily identifiable point sources of dioxin-like compounds. Data on human tissue levels suggest that body burden levels among industrialized nations are reasonably similar. Average background exposure leads to body burdens in the human population which average 40-60 pg TEQ/g lipid (40-60 ppt) when all dioxin-like dioxins, furans and PCBs are included. High-end estimates of body burden of individuals in the general population (approximately the top 10% of the general population) without additional identifiable exposures may be approximately 2 times higher based on available data. While there are some recent data to suggest that both environmental and human body burdens are on a downward trend, additional information will be needed to establish a baseline upon which to evaluate future measurements.

In addition to general population "background" exposure, some individuals or groups of individuals may also be exposed to dioxin-like compounds from discrete sources or pathways locally within their environment. Examples of these "special" exposures include: occupational exposures, direct or indirect exposure to local populations from discrete sources, exposure to nursing infants from mother's milk, or exposures to subsistence or recreational fishers. Although daily exposures to these populations may be significantly higher than daily exposures to the general population, simply evaluating these exposures by averaging higher daily intakes pro-rated over a lifetime might obscure the potential significance of elevated exposures for these sub-populations, particularly if exposures occur for a short period of time during critical times during development and/or growth. This has raised the issue as to the most appropriate "dose metric" to use for dioxin exposure. Exposure levels, intake values, and body burdens have all been used in the past for this purpose. While the current document focusses on body burden, it recognizes that other metrics of exposure may be more appropriate for assessing certain biological responses. In response to a number of comments on this issue, future versions of the report will address this issue more fully.

Mode of Action

This reassessment concludes that the scientific community has identified and described a series of events attributable to exposure to dioxin-like compounds including biochemical, cellular and tissue-level changes in normal biological processes. Binding of dioxin-like compounds to a cellular protein called the "Ah receptor" represents the first step in a series of common biological steps and may be necessary for most if not all of the observed effects of dioxin and related compounds in vertebrates including humans. While binding to the Ah receptor appears to be necessary for all well-studied effects of dioxin, it is not sufficient, in and of itself, to elicit these responses. Many effects elicited by exposure to 2,3,7,8-TCDD are shared by other chemicals which have a similar structure and Ah receptor binding characteristics. This is the main basis for the assumed validity of the TEF approach. Consequently, the biological system appears to respond to the cumulative exposure of Ah receptor-mediated chemicals rather than to the exposure to any single dioxin-like compound. Based on our understanding of dioxin mechanism(s) to date, it is accurate to say that interaction with the Ah receptor is necessary, that the Ah receptor in humans is similar in structure and binding characteristics to those found in dioxin responsive animals, and that there is likely to be a variation between and within species and between tissues in individual species based on differential responses "down stream" from receptor binding. The potency and fundamental level at which these compounds act on biological systems is analogous to several well studied hormones. Dioxin and related compounds have the ability to alter the pattern of growth and differentiation of a number of cellular targets by initiating a series of biochemical and biological events resulting in the potential for a spectrum of responses in animals and humans. Initial simplistic attempts to describe dioxin's mode of action as a transcriptional regulator of gene activity fail to account for recent data that suggests that receptor binding may also alter levels of cellular phosphorylation and hormone and growth factor receptor function without impacting transcription. Further work will be needed to understand this complex of inter-related activities. Additional data available to address these issues will be discussed in revisions to the reassessment document.

The reassessment also finds that there is adequate evidence based on all available information, including studies in human populations as well as in laboratory animals and from ancillary experimental data, to support the inference that humans may have the potential to respond with a broad spectrum of effects from exposure to dioxin and related compounds, if exposures are high enough. These effects will likely range from adaptive changes at or near background levels of exposure to adverse effects with increasing severity as exposure increases significantly above background levels. Enzyme induction, changes in hormone levels and indicators of altered cellular function represent examples of effects of unknown clinical significance and which may or may not be early indicators of toxic response. Induction of activating/metabolizing enzymes at or near background levels, for instance, may be adaptive or may be considered

adverse since induction may lead to more rapid metabolism and elimination of potentially toxic compounds, or may lead to increases in reactive intermediates and may potentiate toxic effects. Demonstration of examples of both of these situations for dioxins and for other families of compounds is available in the published toxicologic literature. Clearly adverse effects including, perhaps, cancer may not be detectable until exposures exceed background by one or two orders of magnitude (10 or 100 times) or more. The mechanistic relationships of biochemical and cellular changes seen at very low levels of exposure to production of adverse effects detectable at higher levels remains uncertain and controversial. It is this relationship in conjunction with an understanding of "background" exposures to dioxin-like compounds that is at the heart of this assessment.

Species Sensitivity

It is well known that individual species vary in their sensitivity to any particular dioxin effect. Human data provide direct or indirect support for evaluation of likely effect levels for several of the endpoints based primarily on animal information although the influence of variability among humans remains difficult to assess. Biochemical, cellular, and organ-level endpoints have been shown to be affected by TCDD, but specific data on these endpoints do not generally exist for other members of this chemical family. Despite this lack of specific data, there is reason to infer that these effects may occur for all dioxin-like compounds, based on the concept of toxicity equivalence.

Some of the effects of dioxin and related compounds such as enzyme induction, changes in hormone levels and indicators of altered cellular function have been observed in laboratory animals and humans at or near body burden levels of people in the general population. Other effects are detectable only in highly exposed populations, and there may or may not be a likelihood of response in individuals experiencing lower levels of exposure. Adverse effects associated with temporary increases in dioxin blood levels based on short term high level exposures, such as those that might occur in animal experiments, an industrial accident or in infrequent contact with highly contaminated environmental media, may be dependent on exposure coinciding with a window of sensitivity of biological processes.

Non-Cancer Health Effects

In TCDD-exposed men, subtle changes in biochemistry and physiology such as enzyme induction, altered levels of circulating reproductive hormones, or reduced glucose tolerance, have been detected in a limited number of the few available studies. These findings, coupled with knowledge derived from animal experiments, suggest the potential for adverse impacts on human metabolism, and developmental and/or reproductive biology, and, perhaps, other effects in the range of current human exposures. Given the assumption that TEQ intake values represent a valid comparison

with TCDD exposure, some of these adverse impacts may be occurring at or within one order of magnitude of average background TEQ intake or body burden levels. It seems reasonable to infer that, as body burdens increase within and above this range, the probability and severity as well as the spectrum of human non-cancer effects most likely increases. It is not currently possible to state exactly how or at what levels humans in the population will respond, but the margin-of-exposure (MOE) between background levels and levels where effects are detectable in humans in terms of TEQs is considerably smaller than previously estimated. These facts and assumptions lead to the inference that some more highly exposed members of the general population or more highly exposed, special populations may be at risk for a number of adverse effects including developmental toxicity based on the inherent sensitivity of the developing organism to changes in cellular biochemistry and/or physiology, reduced reproductive capacity in males based on change in hormone levels and, perhaps, decreased sperm counts, higher probability of experiencing endometriosis in women, reduced ability to withstand an immunological challenge and others. This inference that more highly exposed members of the population may be at risk for various non-cancer effects is supported by observations in animals, by scientific inference, and by some human information from highly exposed cohorts.

The deduction that humans are likely to respond with non-cancer effects from exposure to dioxin-like compounds is based on the fundamental level at which these compounds impact cellular regulation and the broad range of species which have proven to respond with adverse effects. Since, for example, developmental toxicity following exposure to TCDD-like congeners occurs in fish, birds, and mammals, it is likely to occur at some level in humans. It is not currently possible to state exactly how or at what levels people will respond with adverse impacts on development or reproductive function. Fortunately, there have been few human cohorts identified with TCDD exposures in the high end of the exposure range, and when these cohorts have been examined, few clinically significant effects were detected. The lack of adequate human information and the focus of most currently available epidemiologic studies on occupationally, TCDD-exposed adult males makes evaluation of the inference, that non-cancer effects associated with exposure to dioxin-like compounds may be occurring, difficult. It is important to note, however, that when exposures to very high levels of dioxin-like compounds have been studied, such as in the Yusho and Yu-Cheng cohorts, a spectrum of adverse effects have been detected in men, women and children. Some have argued that to deduce that a spectrum of non-cancer effects will occur in humans in the absence of better human data overstates the science; most scientists involved in the reassessment as authors and reviewers have indicated that such inference is reasonable given the weight-of-the-evidence from available data. As presented, this logical conclusion represents a testable hypothesis which may be evaluated by further data collection.

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Development of Margins-of-Exposure (MOE)

The likelihood that non-cancer effects may be occurring in the human population at environmental exposure levels is often evaluated using a "margin-of-exposure" (MOE) approach. A MOE is calculated by dividing the human-equivalent animal LOAEL or no observed adverse effect level (NOAEL) with the human exposure level. MOEs in the range of 100 -1000 are generally considered adequate to rule out the likelihood of significant non-cancer effects occurring in humans based on sensitive animal responses. The average levels of intake of dioxin-like compounds in terms of TEQs in humans described above would result in body burdens well within a factor of 100 of levels representing lowest observed adverse effect levels (LOAELs) in laboratory animals exposed to TCDD or TCDD equivalents. Our analysis of body burdens in animals and humans relative to effect levels for a number of biochemical, cellular and clearly adverse endpoints has recently been published (DeVito, et al.,1995, Environmental Health Perspectives, Volume 103, Number 9) For several of the effects noted in animals, a MOE of less than a factor of ten, based on intake levels or body burdens, is likely to exist. Based on these data alone, traditional toxicologic approaches for deriving likely NOAELs for humans and translating them into "safe" or "tolerable" levels for regulatory purposes will need to be reconsidered. While it is unlikely that any large segment of the human population is incurring an adverse impact from current body burdens, MOEs are less than we once believed. This issue has been recognized by the WHO and an expert panel has recently (November, 1995) been convened to consider the need to re-evaluate the WHO statement regarding a "tolerable daily intake" or TDI for dioxin and related compounds. A report of this meeting will be available in the very near future.

Carcinogenicity of Dioxin-Like Compounds

With regard to carcinogenicity, EPA's weight-of-the-evidence evaluation suggests that dioxin and related compounds (CDDs, CDFs, and dioxin-like PCBs) are likely to present a cancer hazard to humans. Extension of this statement of hazard to this broad range of compounds based on TEFs and in the face of limited data to assess cancer hazard of the individual congeners is a critical issue. The epidemiological data alone are not yet deemed sufficient to characterize the cancer hazard of this class of compounds as being "known." However, combining suggestive evidence of recent epidemiology studies with the unequivocal evidence in animal studies and inferences drawn from mechanistic data supports the characterization of dioxin and related compounds as likely cancer hazards, that is, likely to produce cancer in some humans under some conditions. It is important to distinguish this statement of cancer hazard from the evaluation of cancer risk. The extent of cancer risk will depend on such parameters as route and level of exposure, overall body burden, dose to target tissues, individual sensitivity, and hormonal status.

While major uncertainties remain, efforts of this reassessment to bring more data into the evaluation of cancer potency have resulted in an upper bound, risk specific dose estimate (1 X 10^{-6} risk or one additional cancer in one million exposed) of approximately 0.01 pg TEQ/ kg body weight/ day. Estimates of exposure associated with other specific risk values (10^{-5}, 10^{-4},etc.) can be derived by using a low dose linear model. These risk specific dose estimates represent plausible upper bounds on risk based on the evaluation of animal and human data. These values are similar to previous estimates published by EPA in 1985 but which were based on less data. "True" risks are not likely to exceed these values, may be less, and may even be zero for some members of the population. It is currently not possible to estimate more precisely the risk to exposed individuals. The use of a linear model to provide probabilistic risk estimates remains controversial. Alternative approaches will need to be addressed in future versions of the reassessment. The SAB specifically suggested that the dose-response discussion in Chapter 8 should reflect consideration of alternative models, including those inferring a threshold for response, and their implications on estimates of cancer risk.

The current evidence suggests that both receptor binding and some early biochemical events such as enzyme induction are likely to demonstrate low-dose linearity. The mechanistic relationship of these early events to the complex process of carcinogenesis remains to be established. If these findings imply low-dose linearity in biologically-based cancer models under development, then the probability of cancer risk will be linearly related to exposure to TCDD at low doses, and the slope of the response curve in the low dose region will be a critical issue for predicting risk. If they do not, non-linear relationships may exist between exposures and cancer risk. Until the mechanistic relationship between early cellular responses and the parameters in biologically based cancer models is better understood, the shape of the dose-response curve for cancer in the low-dose region can only be inferred with uncertainty.

Associations between human exposure to dioxin and certain types of cancer have been noted in occupational cohorts with average body burdens of TCDD approximately 2 orders of magnitude (100 times) higher than average TCDD body burdens in the general population. The average body burden in these occupational cohorts level is within 1-2 orders of magnitude (10-100 times) of average background body burdens in the general population in terms of TEQ. Thus, there is no need for large scale low dose extrapolations since these body burdens are the result of occupational exposures added to "background" exposures experienced by the general population. Nonetheless, the relationship of apparent increases in cancer mortality in these populations to calculations of general population risk remains uncertain due to uncertainty in the dose-response relationship within these two orders of magnitude.

TCDD has been clearly shown to increase malignant tumor incidence in laboratory animals (e.g. liver, lung, thyroid, hard palate). It also appears to decrease

the incidence of some hormone-sensitive cancers (uterine, mammary) in laboratory rodents. The reason for this decrease is unknown although some have speculated that it is due to dioxin's anti-estrogenic activity, while others have suggested that it is an indirect consequence of change in animal body weights. In addition, a number of studies analyzed in this reassessment demonstrate other biological effects of dioxin related to the process of carcinogenesis. A number of reviewers including some scientists on the SAB suggest that the complex impacts of dioxin on the carcinogenic process, causing the potential for both increases and decreases in cancer risk in exposed humans, need to be addressed if we are to truly appreciate the impact of dioxin exposures. Initial attempts to construct a biologically-based model for certain dioxin effects as a part of this reassessment will need to be continued and expanded to accommodate more of the available biology relating to potential cancer risk. In addition, biologically-based models to apply to a broader range of potential health effects associated with exposure to dioxin-like compounds will be needed in the future.

Risk Characterization

According to the National Research Council, who articulated the widely used risk assessment paradigm in their seminal, 1983 treatise on risk assessment in the Federal Government, risk characterization is the final step in the risk assessment process in which the first three steps (hazard identification, dose-response assessment and exposure assessment) are summarized and the information integrated to develop a qualitative or quantitative estimate of the likelihood that any of the hazards associated with the agent of concern will be realized in exposed people. In this step, strengths and weaknesses of the available data are discussed, and assumptions and uncertainties which are embodied in the risk assessment are articulated. This guidance has been re-iterated by the EPA in its own risk characterization policy on a number of occasions.

The risk characterization (Chapter 9) for dioxin and related compounds was developed as an integrated analysis of information from the exposure document and from the eight health effects chapters. Key assumptions were identified and discussed. Uncertainties attendant to the findings of the report were highlighted in the integrated analysis and in the risk characterization summary. Issues to be discussed in the risk characterization chapter emerged directly from the previous assessment work carried out by external authors as well as EPA scientists, were articulated by commentors on the process of reassessment in numerous public meetings, and specifically came from recommendations made by peer reviewers of the earlier versions of the reassessment chapters in 1992. This process led to the development of a draft risk characterization, primarily by EPA authors but with the assistance of some outside scientists. This early draft was reviewed extensively within the EPA and by numerous Federal agencies. The inter-agency review resulted in the formation of a drafting team from EPA, HHS, and USDA to address the comments of the reviewers. An unauthorized and unintended release of the inter-agency review draft also produced a round of

unsolicited external comments in June and July, 1994. All of this input formed the basis for the external review draft of the risk characterization which was released in September, 1994 for broad public comment and peer review by the Agency's SAB. Despite the question raised in the charter for this hearing, the risk characterization is consistent with the findings contained in the earlier chapters. Any minor inconsistencies identified by peer review will be rectified in the revised version of the document.

In its October, 1995 report to the Administrator, the SAB noted a number of strengths in the risk characterization. First, "by focusing serious attention on various non-cancer effects, the Agency has dispelled any mis-impression that EPA's risk assessment process is overly preoccupied with carcinogenic effects". Second, "by evaluating an entire group of compound classes (with a common attribute), rather than a single compound, the Agency responds to the generally mistaken criticism that its risk assessment process can only address issues on a chemical-by-chemical basis." Third, "in the opinion of most Committee Members, a useful comparative perspective is provided in the draft conclusions where the Agency highlights the margin of safety (between background exposures and levels of exposure where effects have been seen in test animals) for dioxin-like compounds is smaller than EPA usually sees for many other compounds."

On the other hand, the SAB noted three "major weaknesses." First, "the presentation portrayed in the draft conclusions is not balanced." This statement was footnoted with the following: "Several members of the Committee do not agree with this statement and regard the EPA presentation and the inferences drawn as appropriately conservative within the context of public health protection." Second, "important uncertainties associated with the Agency's conclusions are not fully recognized and subjected to feasible analyses." Third, "the characterization of non-cancer effects is not performed in a manner that allows meaningful analysis of the incremental benefits of risk management alternatives." This statement was footnoted with the following statement: "A minority within the Committee finds the non-cancer risk characterization to be appropriate for use within a public health perspective. However, they agree that the reassessment document's characterization is not performed in a manner which will be very useful in the analysis of the incremental benefits of risk management alternatives by those who will also be concerned with the micro-level incremental costs." These comments with their specified examples as well as more specific comments on the other chapters will be dealt with in the revision process.

Next Steps

The EPA is now in the process of addressing comments on the external review draft of the dioxin reassessment. Comments from the SAB will be considered along with those from the broader scientific community and the public who reviewed the report during the public comment period which extended from September, 1994 to January,

1995. The exposure documents and the first seven chapters of the health assessment document will be revised an updated by EPA Chapter Managers. As suggested by the SAB, summaries are being prepared for each of the health assessment chapters and the contribution of 2,3,7,8-TCDD or other dioxin-like compounds are being delineated so that a greater appreciation of the uncertainty in applying TEQ to complex mixtures can be gained. These revised portions of the document will be subjected to additional internal and limited external peer review prior to being finalized. A disposition of comments will be prepared as the documents are completed. Chapter 8 (Dose-Response Chapter) is being subjected to a major re-write as suggested by the SAB. This re-write will be drafted by an expanded dose-response modeling team, which will include additional statistical expertise and the assistance of a pharmacologist familiar with modeling receptor-mediated responses. The revised Chapter 8 will be subjected to a public peer panel review, containing 8-10 external scientific experts, prior to being finalized, and will be referred back to the SAB for review as suggested. The Risk Characterization will also be extensively revised to address public and SAB comments. As suggested by the SAB, public input on the revision process has been sought, additional experts from outside the Federal government will be enlisted to contribute to the revision, and a public peer review of the revised risk characterization by approximately 10 external scientific experts will be conducted prior to its finalization. The risk characterization will also be referred back to the SAB as suggested. The SAB can then evaluate response to their suggestions and the adequacy of the additional peer review conducted on the draft report.

With regard to the timing of these events, the revision process has already begun. Drafting of chapter summaries and the revised dose response chapter and the risk characterization are anticipated to be complete by March, 1996. Peer panel meetings are expected to be held in early May. Documents will be referred to the SAB in June with a review meeting to be held as soon as possible thereafter. Final documents are targeted for printing in August with release occurring in September, 1996. Obviously, this assumes that no major new issues arise during the revision process that would require extensive additional analysis or obviate the current approach to assessing dioxin risk.

Summary

Based on all of the data reviewed in this reassessment and scientific inference, a picture emerges of TCDD and related compounds as potent toxicants in animals with the potential to produce a spectrum of effects in animals and, perhaps, in humans. Some of these effects may be occurring in humans at very low levels, and some may be resulting in adverse impacts on human health. The potency and fundamental level at which these compounds act on biological systems is analogous to several well-studied hormones. Dioxin and related compounds have the ability to alter the pattern of growth and differentiation of a number of cellular targets by initiating a series of

biochemical and biological events resulting in the potential for a spectrum of responses in animals and humans. Despite this potential, there is currently no clear indication of increased disease in the general population attributable to dioxin-like compounds. The lack of a clear indication of disease in the general population should not be considered strong evidence for no effect of exposure to dioxin-like compounds. Rather, lack of a clear indication of disease may be a result of the inability of our current data and scientific tools to directly detect effects at these levels of human exposure. Several factors suggest a need to further evaluate the impact of these chemicals on humans at or near current background levels. These are: the weight of the evidence on exposure and effects; an apparently low margin-of-exposure for non-cancer effects; and potential for additivity to background processes related to carcinogenicity. Critical issues relating to dioxin exposure and toxicity, and requiring additional attention in the reassessment include: sparse data to derive national means for sources/pathways; state of validation of exposure models; trends in environmental/body burden levels; TEFs/TEQs; impact of human data on hazard and risk characterization; significance of enzyme induction and other biochemical effects; and the relative roles of data, scientific inference, and science policy in informing regulatory decisions. The Agency plans to address comments provided by the general scientific community, the public, and the Agency's SAB. The current schedule, including revision and additional peer review, should allow completion of the dioxin reassessment by September, 1996.

While the science of the reassessment is undergoing further peer review, EPA will be examining the reassessment's policy implications to determine what changes, if any, are needed in existing programs. While regulatory impact assessments are carried out on every regulation that might be issued, no estimates of the economic impact to the public from regulations that may be based on this reassessment have yet been estimated. Throughout the reassessment process EPA has repeatedly stated that existing Agency efforts and programs will not be changed on the basis of this draft reassessment, but they may change significantly after the completion of the report. EPA is committed to developing an Agency-wide strategy for managing dioxin risks, concurrent with completion of the dioxin reassessment. As with the reassessment, we want to provide an opportunity for public input into our policy evaluations. This winter and spring, EPA will hold dioxin policy workshops to explore the policy implications of the reassessment.

Mr. ROHRABACHER. Dr. Gough?

STATEMENT OF MICHAEL GOUGH, PH.D., FORMER GOVERNMENT EXPERT MEMBER OF DIOXIN REASSESSMENT REVIEW COMMITTEE, EPA SCIENCE ADVISORY BOARD

Dr. GOUGH. My light didn't come on. Can you hear me? Okay.

Good morning, Mr. Chairman and committee members. I am Michael Gough, and earlier this year, when I was employed at the Office of Technology Assessment, I was a government expert member of EPA's Science Advisory Board's dioxin reassessment review committee.

I have been involved in analysis and writing about dioxin since 1980, when I was put in charge of OTA's congressionally mandated oversight of executive branch research into possible health effects of exposures to dioxin-contaminated Agent Orange during the Vietnam War.

My book, "Dioxin, Agent Orange," was published in 1986 while I was in the private sector, and I now have a contract to write a second book about dioxin.

I have written a number of papers on this subject, and I chaired a Department of Veterans' Affairs advisory committee about the care of Vietnam veterans, as well as the Department of Health and Human Services committee to review the United States Air Force's ongoing 20-year-long study of the health of the men who sprayed 90 percent of the Agent Orange used in Vietnam.

Mr. ROHRABACHER. What we should do is, that will be a 15-minute bell, if you could proceed with your testimony, as soon as you are done, we will then break to vote and come back and hear the other witnesses.

Dr. GOUGH. Okay.

Mr. ROHRABACHER. Proceed.

Dr. GOUGH. So I should hurry. Okay.

Since OTA closed on September 30, I have accepted a position with the Cato Institute that will begin at the first of the year.

My oral testimony is abstracted from my written text.

The letter of invitation for this hearing mentions four specific issues. I have little to say about two. I do not know why EPA wrote chapter 9, the risk characterization chapter, as well as part of chapter 8 about risk models inhouse, and I do not know why chapter 9 was less extensively peer reviewed than the other chapters before the committee review.

The second issue I will not address is the economic impacts of dioxin regulation.

The first issue that I will discuss is the question about inconsistency between the scientific findings in the earlier chapters and the analyses and conclusions in chapters 8 and 9.

The review committee made numerous comments about such inconsistencies.

To illuminate that point, I will mention some recurring themes in the review committee's report to the SAB.

One, EPA adds together its estimates of the toxicity of all dioxin-like molecules without consideration of antagonistic interactions between and among them.

Moreover, the majority of the committee concluded that PCBs, which account for up to 50 percent of the risk EPA associates with dioxin-like molecules, are sufficiently different from dioxin "that they should not be part of this document."

I must apologize. My references to page numbers are to draft 4(A) of the committee report, which is not the final draft. So you just have to paw through it to find it.

Two, almost all the toxicity data were derived at high dose levels, and EPA inadequately describes its methods for extrapolations to risks at lower doses and provides insufficient justification for its choice of methods.

Three, a molecule present in every cell, the Ah receptor, is considered important to dioxin's mechanism of action but it is not factored into EPA's risk assessment, nor is any other receptor molecule.

Four, had EPA considered a model that includes a receptor molecule, the model would predict a nonlinear and/or a threshold containing dose-response curve. Either of those characteristics would have produced risk estimates lower than those produced by EPA.

Five, EPA classifies dioxin as a complete carcinogen, a molecule capable of causing all the steps that led to cancer.

The committee concludes that dioxin "is not a complete carcinogen and thus to avoid confusion should not be designated as such."

The second issue I will comment about is whether EPA's risk estimates are based on results from exposing animals to high doses of dioxin and extrapolating from those results to estimates of human risk at much lower exposure levels.

In general, that is the case. To a major extent, it is inevitable. If toxic effects are noted in animals, concerns understandably are raised about possible human risk.

The crux of the EPA reassessment is that animal studies indicate that toxic effects can occur at exposures 10 to 100 times above those experienced by humans in the general population.

EPA goes on to say that some segments of the population may be exposed to such levels.

In contrast to EPA's conclusion, the review committee concluded that the only human effect that is "clearly established as being related to TCDD," that is dioxin, "exposure" is chloracne.

That skin disease has been seen only in humans exposed to very high levels of dioxin. It does not result from environmental exposures.

The committee urged EPA to consider carefully the soon to be published results of the Air Force study of the men who sprayed Agent Orange.

As discussed at public meeting in February 1995, only a handful of diseases and possibly clinically significant conditions is elevated in the dioxin-exposed men, and any connection between dioxin and those end points is more of a puzzle than an explanation.

EPA uses two methods to compare animal doses that cause toxic effects to human exposure levels. As can be seen by inspecting EPA's tables in chapter 9, conventional dose-rate comparisons as used by every other agency in government, so far as I know, show that most toxic effects in animals occur at doses 1,000 to 100,000

times higher than human exposure rates, indicating an ample margin of safety for humans.

On the other hand, standing apart from all other agencies in methods of risk estimation, EPA interprets some body burden comparisons that suggest human exposures are much closer to those associated with toxic effects in animals.

The committee asked that EPA review that line of reasoning and justify its decisions.

EPA's summarizing statements are very dramatic. For instance, "It is not currently possible to state exactly how or at what levels humans in the population will respond. But the margin of exposure between background levels and levels where effects are detectable in humans in terms of TEQs," which is a total risk from all dioxin-like molecules, "is considerably smaller than previously estimated."

This statement provides no direction for research or conclusions because of its vagueness. As the committee commented, "The last sentence of the above conclusion, re MOE, is, in the opinion of most, but not all, of the committee, thought to be highly speculative and needs to be reexamined.

In effect, it states that we don't know what will occur or at what level this unknown response will occur, but we know that it will occur in terms of total dioxin exposure closer to background levels than previously estimated."

Another EPA summary statement also drew a specific comment. This is a quote from EPA. "Based on all of the data reviewed in this reassessment and scientific inference, a picture emerges of TCDD," that is, dioxin, "and related compounds as potent toxicants in animals with the potential to produce a spectrum of effects.

Some of these effects may be occurring in humans at very low levels, and some may be resulting in adverse impact on human health."

As the committee reports states, "It is difficult to determine what EPA is inferring in the last sentence of the above-cited conclusion.

If it is intended to state that adverse effects in humans may be occurring at near current exposure levels, it is the committee's judgement that EPA has not submitted findings that support adequately this conclusion."

I want to thank you for this opportunity to testify, and I will be happy to answer any questions.

[The prepared statement of Dr. Gough follows:]

Testimony of Michael Gough, PhD*

before the

Committee on Science

U.S. House of Representatives

December 13, 1995

* Government expert member of Dioxin Reassessment Review Committee of the EPA Science Advisory Board.

Good morning, Mr. Chairman and Committee members. I am Michael Gough, and earlier this year, when I was employed at the Office of Technology Assessment, I was a government expert member of EPA's Science Advisory Board's Dioxin Reassessment Review Committee. I have been involved in analysis and writing about dioxin since 1980 when I was put in charge of OTA's congressionally mandated oversight of Executive Branch research into the possible health effects of exposures to dioxin-contaminated Agent Orange during the Vietnam war. My book Dioxin, Agent Orange was published in 1986, while I was in the private sector, and I now have a contract to write a second book about dioxin. I have written a number of papers about dioxin, and I chaired a Department of Veterans Affairs Advisory Committee about the care of Vietnam veterans and the Department of Health and Human Services Committee to review the United States Air Force's on-going 20-year-long study of the health of the men who sprayed 90 percent of the Agent Orange used in Vietnam. Since OTA closed on September 30, I have accepted a position at the Cato Institute that will begin at the first of the year.

The letter of invitation for this hearing mentions four specific issues to be considered. I have little to say about two of those: I do not know why EPA wrote chapter 9, the Risk Characterization Chapter (and part of chapter 8 about risk models) in-house, and I do not know why chapter 9 was less extensively peer reviewed than the other chapters before the committee review. Nevertheless, the statement in the invitation letter that the

chapter was not peer reviewed appears too absolute. I have seen comments on an earlier draft of chapter 9 that were written at the U.S. Department of Agriculture and at the Food and Drug Administration. The second issue that I will not address is the economic impacts of dioxin regulation.

The first issue that I will discuss is the question about inconsistency between the scientific findings in the earlier chapters and the analyses and conclusions in chapters 8 and 9. The review committee made numerous comments about such inconsistencies. To illuminate that point, I will mention some recurring themes in the review committee's report to the SAB:

1. EPA adds together its estimates of the toxicity of all dioxin-like molecules, without consideration of antagonistic interactions between and among them. The compounds other than the one commonly called "dioxin" account for 90 percent of EPA's risk estimate, and hardly anything is known about any of them. Moreover, a majority of the committee concluded that PCBs, which account for up to 50 percent of the risk EPA associates with dioxin-like molecules are "sufficiently different from ... [dioxin] ... that polyhalogenated biphenyls [PCBs and related molecules] not be a part of this document" (p. 59).

2. Almost all the toxicity data were derived at high dose levels, and EPA inadequately describes its methods for extrapolation to risks at lower doses and provides insufficient justifications for its choice of methods.

3. A molecule present in every cell -- the Ah receptor -- is

considered important to dioxin's mechanism of action, but it is not factored into EPA's risk assessment (nor is any other receptor molecule). On the other hand, the committee also criticized EPA for invoking the initial binding of dioxin to the Ah receptor as a harbinger of many toxic effects with no evidence for any connection and no knowledge of any kinetics between the binding and the effect.

4. Had EPA considered a model that includes a receptor molecule, the model would predict a non-linear and/or a threshold containing dose response curve. [Either of those characteristics would have produced risk estimates lower than those produced by EPA.]

5. EPA classifies dioxin as a complete carcinogen -- a molecule capable of causing all the steps that lead to cancer. The committee concludes that dioxin "is not a complete carcinogen and thus to avoid confusion should not be designated as such" (p. 65). [This is an important distinction because low level exposures to incomplete carcinogens, in most people's minds, is much less risky than exposure to complete carcinogens.]

The committee report is full of criticisms, but it also praises EPA in some places. In general, however, the praise was given to summaries and reviews of data, and the criticisms were addressed at the risk characterization.

The second issue that I will comment about is whether EPA's risk estimates are based on results from exposing animals to high doses of dioxin and extrapolating from those results to estimates

of human risk at much lower exposure levels. In general, that is the case. To a major extent, it is inevitable. When toxic effects are noted in animals, concerns, understandably, are raised about possible human risks.

EPA used human data to discount possible associations between dioxin and many human cancers. Both EPA and the committee fix on soft tissue sarcomas as the only human tumor that can reasonably be associated with dioxin. [I disagree with that association, and I fully expect that it will weaken with the passage of time and careful consideration of available data and new data that will become available.]

The crux of the EPA reassessment is that animal studies indicate that toxic effects can occur at exposures 10- to 100-times above those experienced by humans in the general population. EPA goes on to say that some segments of the population may be exposed to such levels.

In contrast to EPA's conclusion that segments of the population might be suffering multiple adverse effects from dioxin exposures, the review committee concluded that the only human effect that is "clearly established as being related to TCDD [dioxin] exposure" is chloracne [p. 55]. That disease has been seen only in humans exposed to very high levels of dioxin; it does not result from environmental exposures.

The committee urged EPA to consider carefully the soon-to-be published results of the Air Force study of the men who sprayed Agent Orange. The current concentrations of dioxin in the bodies

of those thousand men are known, and the data provide a rich source of information. As discussed at a public meeting in February 1995, only a handful of diseases and possibly clinically significant conditions is elevated in the dioxin-exposed men, and the connection between dioxin and those endpoints is more of a puzzle than an explanation. EPA's examination of the Air Force data and data from other studies of dioxin-exposed humans should enable the agency to compare its estimates from animal studies to measurements in humans.

EPA uses two methods to compare animal doses that cause toxic effects to human exposure levels. The first is the conventional method, used by all other agencies and governments, that compares the amount of dioxin inhaled or ingested per unit of body weight per day. The other is a comparison of the average concentration of dioxin in an adult human after a life-time of low-level exposure to the (usually estimated) concentration in animals following a single exposure or exposure of a few weeks to much-higher-than-human exposures.

As can be seen by inspecting EPA's tables in chapter 9, conventional dose rate comparisons show that most toxic effects in animals occur at doses 1000 to 100,000-times higher than human exposure rates, indicating that there is an ample margin of safety for humans. On the other hand, EPA interprets some body burden comparisons to suggest human exposures are much closer to those associated with toxic effects in animals. The committee asked that EPA review that line of reasoning and justify its decisions.

EPA's summarizing statements are very dramatic: For instance,

> It is not currently possible to state exactly how or at what levels humans in the population will respond, but the margin of exposure (MOE) between background levels and levels where effects are detectable in humans in terms of TEQs [total risk from all dioxin-like molecules] is considerably smaller than previously estimated. (Chapter 9, p. 81)

This statement provides no direction for research or conclusions because of its vagueness. As the committee commented:

> The last sentence of the above quoted conclusion (re MOE) is (in the opinion of most, but [not] all of the Committee) thought to be highly speculative and needs to be reexamined. In effect, it states that we don't know what will occur or at what level this unknown [response] will occur, but we know that it will occur (in terms of TEQs) closer to background levels than previously estimated (p. 92).

Another EPA summary statement also drew a specific comment:

> Based on all of the data reviewed in this [dioxin] reassessment and scientific inference, a picture emerges of TCDD [dioxin] and related compounds as potent toxicants in animals with the potential to produce a spectrum of effects. Some of these effects may be occurring in humans at very low levels, and some may be resulting in adverse impacts on human health (Chapter 9, p. 87).

As the committee report states,

> It is difficult to determine what EPA is inferring in the last sentence in the above cited conclusion. If it is intended to state that adverse effects in humans may be occurring near current exposure levels, it is the Committee's judgement that EPA has not presented findings that support adequately this conclusion (p. 94).

I want to thank you for this opportunity to testify, and I will be happy to answer any questions.

Mr. ROHRABACHER. Dr. Gough, thank you very much.

And we will recess now until after this first vote. Thank you very much.

[Brief recess.]

Mr. ROHRABACHER. This hearing is called to order.

Dr. Lucier, would you like to proceed?

STATEMENT OF GEORGE W. LUCIER, PH.D., DIRECTOR, ENVIRONMENTAL TOXICOLOGY PROGRAM, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

Dr. LUCIER. Thank you. Good morning. I am George Lucier, director of the environmental toxicology program at the National Institute of Environmental Health Sciences, one of the 17 institutes of the National Institutes of Health.

My research on dioxin is attempting to identify and fill knowledge gaps which create uncertainty in risk assessment.

These findings are published frequently in the peer reviewed scientific literature. Of my roughly 200 publications, scientific publications, about one third of them deal wholly or in part with dioxin.

My involvement with EPA's reevaluation of dioxin's risks has spanned nearly four years and contributed to the preparation of two of the nine chapters constituting the health effects document.

The reevaluation of dioxin's risks by EPA represents the most visible effort by a U.S. regulatory agency to move away from default methodologies and to incorporate all relevant information in the decision process.

The use of information on mechanism is an important step in reducing uncertainty.

I would now like to comment on specific scientific issues within the framework of risk assessment for dioxin and related chemicals.

Regarding hazard identification, dioxin causes a number of adverse effects in experimental animals, and some of these effects have been associated with high dioxin exposure in humans.

In regard to cancer, 17 studies have been conducted in rodents and all are positive——

Mr. ROHRABACHER. Excuse me. Could you please repeat what you just said a few moments just before that?

Dr. LUCIER. In regard to cancer?

Mr. ROHRABACHER. In animals and in humans. Because that is something that has been disputed, I think.

Dr. LUCIER. It says dioxin causes a number of adverse effects in experimental animals, and some of those effects have been associated with high dioxin exposure in humans.

Mr. ROHRABACHER. Okay. Could you tell me what that means? And then you could go on.

Dr. LUCIER. That means that when you look at dioxin body burden, say, from an environmental or occupational exposure and look at cancer incidence in the population that has those burdens, there is an association between the two; dioxin concentrations, which, in this case, as I had said, were high, and that adverse outcome, such as cancer.

Mr. ROHRABACHER. In terms of the relationship between how it affects animals and humans.

Dr. LUCIER. My statement merely was that dioxin causes cancer in experimental animals.

Mr. ROHRABACHER. Right.

Dr. LUCIER. And there is an association with high dioxin exposures in humans either from environmental or occupational settings and cancer in humans. This doesn't prove that dioxin is causing that cancer, it merely says that there is an association.

Mr. ROHRABACHER. Right.

Dr. LUCIER. Which means that the——

Mr. ROHRABACHER. In other words, the same dioxin that caused the cancer in the animals causes the health impact on humans in a high dose.

Is that what you're saying?

Dr. LUCIER. Yes.

Mr. ROHRABACHER. Okay. Go right ahead. Sorry.

I just wanted to make sure I understood that exact point.

Dr. LUCIER. Okay.

And I will say my next sentence even though it reiterates what I just said. Epidemiology studies on humans exposed to dioxin at high doses provide evidence that dioxin is a human carcinogen, although the influence of confounding factors cannot be entirely ruled out.

Dioxin also produces a number of noncancer effects in experimental animals, such as birth defects, reproductive problems, neurologic disorders, and hormonal alterations.

Recent studies in humans suggest that some noncancer effects may also occur in humans exposed to high doses.

Dioxin also causes a vast array of hormonal, molecular, and biochemical effects, some of which are likely involved in the adverse health effects.

It has been called, with good reason, an environmental hormone or endocrine disruptor.

My bottom line on hazard identification are that dioxin should be considered a probable human carcinogen and that noncancer effects of dioxin and related compounds are a public health concern.

Current estimates are that adults in the U.S. are exposed to approximately 10 picograms of the prototypical dioxin TCDD every day.

For reference, this amount is equivalent to about one-trillionth of an ounce. Dioxin exposure in the general population comes primarily from consuming contaminated foodstuffs.

The current average exposure levels of American adults is 10 to 20 times higher than the exposure level that EPA estimates could cause up to one cancer in a million people exposed over their lifetimes.

EPA and other risk assessors acknowledge that the actual risk could very well be lower.

Human risk estimates should include an evaluation of numerous other environmental chemicals that act through the same mechanism as TCDD. For example, there are 75 different dioxins and over 100 different chlorinated dibenzofurans and some dioxin-like PCBs.

Dioxin is a persistent chemical in the human body and in the environment. For example, a biological half-life of dioxin in humans is 7 to 109 years.

Dioxin is found preferentially in fat, which means that fatty tissues and human milk contain significant amounts of dioxin.

Based on human milk concentration data, newborns who breastfeed for 6 to 12 months receive a dose of dioxin while nursing approximately 15 times higher than the average adult in the United States. Although this exposure level is of concern, the benefits of breastfeeding certainly outweigh the risk.

The summary of my comments on human exposure is that everyone has some dioxin in their bodies and, because of its biological persistence, everyone alive today will retain dioxin in their bodies through their lifetimes even if their exposures cease now.

The component of risk assessment that generally creates the most uncertainty is dose-response evaluation, and dioxin is no exception.

While there is considerable data to support the claim that dioxin produces adverse health effects in humans, at least at high doses, there is legitimate scientific debate regarding health effects at lower doses.

What is needed is the development of credible biologically based models for estimating human risk from exposure levels encountered from day-to-day living.

There has been debate regarding the relevance of rodent data in estimating human risk. I believe that there is considerable evidence to support the use of rodent data.

First, rat or mouse cells, like human cells, contain the Ah receptor, which is necessary for most, if not all, of dioxin's effects.

Second, the amount of dioxin-like, chemicals required to elicit changes in gene expression, is approximately the same in both rats and humans.

Third, the spectrum of toxic effects is somewhat similar in rats and humans. However, the half-life of dioxin in rats is 25 days compared to 7 to 10 years in people.

This means that if rats and humans each had equivalent doses of dioxin for 2 years, daily doses, humans would have 100 times more dioxin in their bodies than would rats. This needs to be factored in when using rodent data to estimate human risk.

In summary, EPA has asked for and received considerable input from the scientific community in their reevaluation of dioxin's risks.

This information raises concerns about current levels of human exposure to dioxin and dioxin-like chemicals. EPA's risk characterization, I believe, is correct in expressing that concern.

This conclusion is based on information present in the background chapters which were peer reviewed in 1992 and '93.

However, this statement does not mean that adverse health effects have been shown to occur as a consequence of current exposures of the general population of the U.S.

The risk characterization does suffer from the need to condense 2,000 pages of background into a 50-page characterization.

The selection of supporting information may have caused some of the concerns expressed by the Science Advisory Board.

This ongoing review, as documented by Dr. Farland, when completed, should improve the risk characterization chapter.

Finally, EPA's reevaluation of dioxin's risk has been and remains a daunting task. I believe that EPA has conducted an extraordinarily open and scientifically based assessment.

Thank you.

[The prepared statement of Dr. Lucier follows:]

Testimony of George W. Lucier, Ph.D.
Director
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Before the House Committee on Science
Subcommittee on Energy and Environment

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Good morning, I am Dr. George Lucier, Director of the Environmental Toxicology Program at the National Institute of Environmental Health Sciences (NIEHS), one of 17 institutes at the National Institutes of Health (NIH). I have conducted research at NIEHS for 25 years and have published nearly 200 papers in the peer-reviewed scientific literature. Roughly 1/3 of them address wholly, or in part, health effects of dioxin. My current research on dioxin and related chemicals is attempting to identify and fill knowledge gaps which create uncertainty in risk assessment. These studies are multidisciplinary and attempt to integrate data from experimental systems, human samples and molecular mechanisms of action.

My involvement with EPA's reevaluation of dioxin's risks has spanned nearly four years and has contributed to the preparation of two of the nine chapters constituting the health effects documents. I was the lead author of the "Carcinogenicity" chapter, and I co-chaired the committee with Dr. Mike Gallo (Environmental and Occupational Health Sciences Institute of New Jersey) that prepared Chapter 8 on "Dose Response Evaluations." I also served on a Department of Health and Human Services (DHHS) committee which reviewed a preliminary draft of Chapter 9, the "Risk Characterization" chapter. The Public Health Service has played a key role in evaluating human health consequences from dioxin and in the risk communications part of the reassessment and has worked with EPA on this issue.

General Issues

The purpose of the reevaluation was to use new information on dioxin's mechanism of action to improve estimates of risks at various exposure levels. The centerpiece of the reevaluation reflects the general scientific consensus that most, if not all, of dioxin's effects are mediated by a cellular receptor, which functions in a manner analogous to receptors for steroid hormones. I will come back to this receptor system later in my testimony. I believe that EPA has been extraordinarily thorough in involving the best scientific minds in the reevaluation process as chapter authors, members of peer-review panels for individual chapters, or as ad hoc members of the Science Advisory Board's review of the reevaluation document. It is safe to say that most of the top scientists in the dioxin arena have been involved in one way or another.

The reevaluation of dioxin's risks by EPA represents the most visible effort by a U.S. regulatory agency to move away from default methodologies for estimating human risks and to incorporate all relevant scientific information in the decision process. Clearly, we don't know all that we would like to know about dioxin, and clearly uncertainty will remain in human risk estimates. The use of information on mechanism is a very important step in reducing uncertainty. Efforts such as this one will help restore public confidence in regulatory actions.

I would now like to comment on specific scientific issues within the framework of risk assessment that impact on human health effects of dioxin and related chemicals.

Hazard Identification

Dioxin causes a number of adverse effects in experimental animals and some of those effects have been associated with high dioxin exposures in humans. In regard to cancer, 17 studies have been conducted in rodents and all are positive. Epidemiology studies on humans exposed occupationally or accidentally to dioxin at high doses provide evidence that dioxin is a human carcinogen although the influence of confounding factors cannot be entirely ruled out. Dioxin also produces a number of non-cancer effects in experimental animals such as birth defects, reproductive problems, neurologic disorders, and hormonal alterations, some of which occur at low doses. Recent studies in humans suggest that some non-cancer effects may also occur in humans exposed to high doses. In addition to adverse health effects, numerous studies in the scientific literature demonstrate that dioxin causes a vast array of hormonal, molecular, and biochemical effects some of which are likely involved in the adverse health effects described above. It has been called, with good reason, an environmental hormone or endocrine disrupter. I will come back to dioxin's effects later in my comments on dose-response relationships.

As I mentioned earlier, it is generally accepted by the scientific community that most, if not all, of dioxin's effects require an initial interaction with a cellular protein called the Ah receptor. The Ah receptor, when bound to dioxin, can trigger changes in the function of genes, and it is those changes that most scientists think are an early and necessary event in the ability of dioxin to cause cancer and non-cancer effects. However, our knowledge of the precise way that changes in gene expression lead to toxicity is far from complete. It is this knowledge gap that creates much of the uncertainty in risk estimation at low exposure

levels.

My bottom lines on hazard identification are that dioxin should be considered a probable human carcinogen and that non-cancer effects of dioxin and related compounds are of public health concern.

Exposure Assessment

Dioxins are produced in a number of ways. The key point is that the opportunity for dioxin production and contamination is present whenever heat, chlorine, and organic materials are together. The most notable historical sources of dioxin have been contamination of herbicides (e.g. agent orange), emissions from incinerators, and bleaching of paper although it should be noted that American paper industries have developed and applied new technology to dramatically decrease dioxin emissions during the paper-bleaching process.

Current estimates are that adults in the U.S. are exposed to approximately 10 picograms of the prototypical dioxin, 2,3,7,8-tetrachloro-dibenzo-p-dioxin (TCDD) every day. For reference, this amount is equivalent to about 1 trillionth of an ounce. Although this number is very small, dioxin is an extraordinarily toxic chemical. Dioxin exposure comes primarily from consuming contaminated foodstuffs. Current average exposure levels of American adults is 10-20 times higher than the exposure level that EPA estimates could cause up to one cancer in a million people exposed over their lifetimes. EPA and other risk assessors acknowledge that this cancer risk estimate is clearly conservative, and that the actual risk could very well be lower.

It is important to recognize that human risks from dioxin must include an evaluation of

numerous other environmental chemicals that act through the same mechanism as TCDD. For example, there are 75 different dioxins, over 100 different structurally related chlorinated dibenzofurans and some dioxin like polychlorinated biphenyls (PCBS). In addition, brominated analogs of dioxins and furans are environmental contaminants. Toxicity of these chemicals appears to be proportional to the strength of their binding to the Ah receptor and the length of time that the chemical remains in the body. Thus, when appropriate scientific information is available, it is possible to calculate the total exposure to dioxin-like compounds and estimate risks of that exposure. Using this approach, it appears that only 5-10% of our exposure to dioxin-like chemicals is from the prototypical dioxin, TCDD. In other words, the average person is exposed to the equivalence of 100-200pg dioxin per day.

Dioxins are persistent chemicals in the human body and in the environment. For example, the biological half life of dioxin in humans is 7-10 years. This means that if two molecules of dioxin enter your body today, one will be left 7-10 years from now. Dioxin is found preferentially in fat which means that fatty tissues and human milk contain significant amounts of dioxin. Based on human milk concentration data, newborns who breast feed for 6-12 months, receive a dose of dioxin, while nursing, approximately 15 times higher than the average adult in the United States. Although, this exposure level is of concern, the benefits of breast feeding certainly outweigh the risks.

The summary of my comments on human exposure is that human exposure to dioxins is broad-based (everyone has some dioxin in their bodies), and because of its biological persistence, everyone alive today will retain dioxin in their bodies for their lifetimes, even if

their exposure ceased now.

Dose-Response Evaluation

The component of risk assessment that generally creates the most uncertainty is dose-response evaluation, and dioxin is no exception. While there is considerable data to support the claim that dioxin produces adverse health effects in humans, at least at high doses, I believe that there is legitimate scientific debate regarding health effects at lower doses. Data from experimental systems provide evidence that dose-response relationships for dioxin's effects on gene expression are likely linear; that is a proportional relationship appears to exist between exposure level and effect over a wide dose range. Therefore, it is fairly straightforward to estimate the magnitude of these kinds of responses outside the range of observable data. If we were confident that health effects caused by dioxin exhibited the same dose-response relationships as changes in gene expression, then risk assessment would be easy. A linear model would estimate risk with reasonable certainty. However, this is not the case. Our laboratory and others have shown that dose-response relationships for complex responses such as disease are different than those for changes in gene expression. We are conducting research to better understand the molecular and biological determinants of dose response, but we do not yet have the answer. Neither linear models nor threshold models (assume that there is an exposure level below which no effect occurs) are based on a solid scientific base. What is needed is the development of credible biologically-based models for estimating health risks from exposure levels encountered from day-to-day living. This effort should work towards such models for both cancer and non-cancer effects since it could be that adverse outcomes such as reproductive toxicity occur at lower exposure levels

than cancer.

Relevance of Animal Models for Estimating Human Risks

There has been considerable debate regarding the relevance of rodent data in estimating human risks. I believe that there is convincing evidence to support the use of rodent data. First, rat or mouse cells, like human cells, contain the Ah receptor which, as discussed earlier, appears essential for dioxin responses. Second, the amount of dioxin-like chemicals required to elicit changes in gene expression is approximately the same in both rats and humans. The human data has been obtained from people who were occupationally or accidentally exposed to dioxin. Third, the spectrum of toxic responses caused by dioxin in rats is similar to the spectrum of toxic effects associated with dioxin exposure in humans including cancer and reproductive parameters. The problem is that we don't have adequate data to determine low-dose adverse effects in rats although good data on molecular effects is available. I am reasonably confident, however, that the rat is an appropriate model for estimating human risks with one exception; that is, rodents clear dioxin from their bodies much more rapidly than observed in people. The half-life of dioxin in rats is 25 days compared to 7-10 years in people. This means that the chronic exposure level which produces a given body burden of dioxin in humans is approximately 100 times lower than that needed to produce the same tissue burden in rats. Conversely, if rats and humans each had the same daily intake of dioxin for two years, humans would have 100 times more dioxin in their bodies than would rats. This needs to be factored in when using rodent data to estimate human risks.

Summary

EPA has asked for and received considerable input from the scientific community in their reevaluation of dioxin's risk. Taken together, information on human exposures and health effects, experimental studies and levels of environmental contamination provide evidence that we should be concerned about current levels of human exposure to dioxin and dioxin-like chemicals. EPA's risk characterization, I believe, is correct in expressing that concern. This conclusion is supported by information present in the background chapters which were peer-reviewed in 1992 and 1993. However, this statement does not mean that adverse health effects have been shown to occur as a consequence of current exposures of the general population in the United States. The risk characterization does suffer from the need to condense 2000 pages of background into a 50 page characterization. The selection of supporting information may have caused some of the concerns expressed by the Science Advisory Board. This ongoing review when completed should improve the risk characterization chapter. Finally, EPA's reevaluation of dioxin's risks has been and remains a daunting task. EPA should be commended for conducting an extraordinary open and scientifically-based assessment.

Mr. ROHRABACHER. Thank you very much.
Dr. Jones?

STATEMENT OF KAY JONES, PH.D., PRESIDENT, ZEPHYR CONSULTING, SEATTLE, WASHINGTON

Dr. JONES. Mr. Chairman, members of the committee, thank you for the opportunity to testify regarding EPA's dioxin reassessment.

My comments are in response to the hearing charter.

I have been involved in the risk assessment of dioxin impacts for some 15 years, have been closely involved in the whole reassessment process as a peer reviewer.

Although I am in almost complete agreement with the EPA Science Advisory Board's review findings, I would like to discuss some other fundamental problems with the EPA's reassessment documentation and its premature use in setting emissions control policy and the agency's issuance of regulatory orders.

Some specific examples which illustrate my concerns are as follows:

EPA claimed at their regional office public announcements in September 1994 that it was seeking public input and peer review of the reassessment documents.

If this were the case, why were EPA spokespersons clearly stating that hospital and municipal waste incinerators were major contributors to current human dioxin exposure? Why did the same spokesperson suggest that a low beef consumption diet was an appropriate health protection measure?

This preemption of the peer review process would be unacceptable outside of government.

EPA's reassessment stated that dioxin-like PCBs are a major contributor to our current body burden of dioxin-like compounds.

Despite the significance of this contribution, the reassessment failed to address PCB exposure in a balanced fashion relative to dioxins.

EPA's ORD staff conducted a screening risk assessment of an existing waste energy facility in Columbus, Ohio, based on a methodology which was still under peer review. EPA Region 6 issued a regulatory order stating that the risk assessment results demonstrated a probable imminent health endangerment to the community in Columbus, Ohio, creating hysteria among some citizens.

Not only was the risk assessment result grossly exaggerated, the use of such RAs for imminent health endangerment declarations is totally inappropriate.

Despite numerous appeals by the Solid Waste Authority of Central Ohio, EPA has refused to withdraw that risk assessment.

EPA was engaging in the setting of overly strict standards on the dioxin emissions from hospital incinerators during the reassessment review process, touting such emissions as being the biggest single identified source in the United States.

Although the SAB pointed out that this estimate was probably high, based on new information, this was not the fact of the matter.

It should have been impossible to make a 10- to 50-fold overestimate, given the availability of the requisite data prior to September 1994.

This example underscores a lack of internal checks on the technical validity of EPA staff work.

EPA did not carry out a good-faith effort to inventory known sources of dioxin emissions as the SAB politely suggested.

The European inventories contain many more sources which are also common to the U.S. but were ignored by EPA. It appeared to me that EPA has a pre-set agenda to emphasize the contribution of waste incineration while downplaying or ignoring other obvious or potential sources.

EPA fully recognized the sensitivity of risk assessment results to its new proposed model relating dioxins in air to dioxins in grass and beef in 1992.

It caused previous site-specific risk assessment cancer estimates to increase 100- to 10,000-fold. This conceptual model result was used by plaintiffs in the infamous East Liverpool, Ohio, hazardous waste incinerator test burn hearing that EPA has not conducted any field measurements since 1992 to verify this model which links unknown rural air levels of dioxins to our beef supply.

More recent data from European research strongly suggests that EPA's new air-to-beef pathway model is no more significant than what was modeled prior to the issuance of the reassessment.

I think the major misconception that the authors of chapter 9 have is that they believe that they have applied the best science at hand in developing policy and taken regulatory actions prior to the orderly completion of the risk assessment process.

They should understand that the technical hypotheses produced by EPA, or by any researcher, for that matter, are not a contribution to science until they have been thoroughly peer reviewed.

Good policy can only be based on good science. It cannot be based on anecdotal information or personal biases.

I firmly believe that EPA should be a risk-based agency.

In fact, most of EPA's past regulatory decisions took risk into account in some fashion. The dilemma is how good are EPA risk assessment procedures? This is doubly important when EPA staff attempt to misapply existing scientific work.

Poor policies will always emerge from poor risk assessments, as clearly demonstrated so far in the dioxin case.

The major issue is how can we ensure that the agency conducts scientifically valid and balanced risk analyses in the future?

Some form of a strict peer review procedure must be required if the risk assessment and regulatory functions are to remain in the same agency.

Thank you.

[The prepared statement of Dr. Jones follows:]

Testimony of
Kay H. Jones Ph.D.
before the
Subcommittee on Energy and Environment
of the
Committee on Science
U.S. House of Representatives
December 13, 1995

Thank you for the opportunity to testify regarding EPA's dioxin reassessment. My comments are in response to the four issues set forth in the Hearing Charter. I have been involved in the risk assessment (R/A) of dioxin impacts for some fifteen years and have been closely involved in the whole reassessment process as a peer reviewer. Although I am in almost complete agreement with the EPA Science Advisory Board's review findings, I would like to discuss other fundamental problems with EPA's reassessment documentation and its premature use in setting emissions control policy and the Agency's issuance of regulatory orders. Some specific examples which illustrate my concerns are as follows:

• EPA claimed at their 10 regional office public announcements in September 1994 that it was seeking public input and peer review of the reassessment documents. If this were the case why were the EPA spokespersons clearly stating that hospital and municipal waste incineration were major contributors to current human dioxin exposure? Why did these same spokespersons suggest that a low beef consumption diet was an appropriate health protection measure? This grandiose preemption of the peer review process would be unacceptable outside of government.

• EPA's reassessment stated that dioxin like PCBs are a major contributor to our current body burden of dioxins. (They in fact misused the research paper in making its estimate of the PCB contribution. Actually more than a 50% contribution as opposed to the 30% contribution reported by EPA.) Despite the significance of this contribution, the reassessment failed to address the PCBs in a balanced fashion relative to dioxins.

• EPA's validation of the air to beef model was addressed by the SAB, suggesting that the air-plant-animal pathway..."is a worthwhile hypothesis and may well be true...it can not be proved at this time." This statement clearly questions the claim that they have a valid model. In fact, the papers they have published which attempt to show model agreement with observed data do not employ statistical methods required by EPA superfund regulations. Despite these issues, EPA still used the model for regulatory purposes.

• EPA ORD staff conducted a screening risk assessment of an existing waste to energy facility in Columbus Ohio based on the unvalidated air to beef model which was still under peer review. EPA Region V issued a regulatory order stating that the R/A results demonstrated imminent health endangerment to the community in Columbus, creating hysteria among some citizens. Not only was the R/A result grossly exaggerated, the use of such R/As for an imminent health endangerment declaration is totally inappropriate. Despite numerous appeals by the Solid Waste Authority of Central Ohio, EPA has refused to withdraw the R/A.

• EPA was engaging in the setting of overly strict standards on the dioxin emissions from hospital waste incinerators during the reassessment review process, touting such emissions as the biggest single source in the U.S., i.e., 5100 out of 9300 gms toxic equivalence (TEQ). Although the Science Advisory Board (SAB) pointed out that this estimate was probably high based on new information this was not the fact of the matter. EPA had every opportunity during the development of its inventory to conduct an unbiased emission inventory of this class of waste incinerators, but failed to do so. It should have been impossible to make a 10 to 50 fold error given the availability of the requisite data prior to Sept. 1994. This example underscores the lack of internal checks on the technical validity of staff work. This is only one among many that I documented during my peer review of the exposure chapters.

• EPA did not carry out a good faith effort to inventory known sources of dioxin emissions as the SAB had politely suggested. European inventories contained many more sources which are also common to the U.S. but were ignored by EPA. It appeared to me that EPA had a preset agenda to emphasize the contribution of waste incineration while down playing or ignoring other obvious sources, e.g., iron sintering plants, secondary aluminum smelting, etc.. Although they appeared to weigh the possible uncertainty of estimates for different sources they failed to apply their criteria in an even handed manner to all potential sources. The potential

contribution of diesel fueled mobile sources is a prime example. They also did not discuss the potential exposure differences among the sources they did inventory. For example, 24 municipal waste incinerators were responsible for more than 90% of this source categories total inventory. It is difficult to logically relate such a few isolated sources to impacts on our U.S. beef industry.

• EPA fully recognized the sensitivity of R/A results to its new proposed model relating dioxins in air to dioxins in grass and beef in 1992. It caused previous site specific R/A cancer risk estimates results. to increase 100 to 10,000 fold. This conceptual model result was used by plaintiffs in the infamous East Liverpool hazardous waste incinerator test burn hearing. EPA has modified this model protocol on at least three occasions prior to the issuance of the reassessment and once this past summer. All of these changes reflected progressively lower risks associated with the air to beef transfer of dioxins. Yet EPA has not conducted any field measurements since 1992 to verify this model which links unknown rural air levels of dioxins to our beef supply. More recent data from European research strongly suggests that EPA's "new air to leaf to beef pathway" is no more significant than what was modeled prior to the issuance of the reassessment.

I think the major misconception that the authors of Chapter 9 have is that they believe they have applied the best science at hand in developing policy and taking regulatory actions prior to the orderly completion of the reassessment process. They should understand that technical hypotheses produced by EPA or by any researcher for that matter are not a contribution to science until they have been thoroughly peer reviewed. Good policy can only be based on good science. It cannot be based on anecdotal information or personal biases.

I firmly believe that EPA should be a risk based agency. In fact, most of EPA's past regulatory decisions took risk into account in some fashion. The dilemma is how good are EPA risk assessment procedures. This is doubly important when EPA staff attempt to misapply existing scientific work. Poor policies will always emerge from poor risk assessments as clearly demonstrated so far in the dioxin case. The major issue is how can we insure that the agency conducts scientifically valid and balanced risk analyses in the future. Some form of a strict peer review procedure must be required if the risk assessment and regulatory functions are to remain in the same agency.

Mr. ROHRABACHER. Thank you very much, Dr. Jones.

And I am going to ask one question myself. You know, we are looking at this assessment and its reassessment.

And that is, and I hate to put Dr. Farland on the spot because you are the one who is actually in charge of what everybody is talking about here. So you are going to get most of the heat in this hearing, although that is not the purpose to put you on the hot spot, but to discuss how you do your job.

And let me ask you. Why was there a different peer review process for the final chapter, I guess, or chapters than for the rest of that reassessment?

Dr. FARLAND. Mr. Chairman, we laid out the process that we were going to use to for the reassessment back in 1991 and '92 and detailed that quite extensively with the public.

The approach that we decided to use was——

Mr. ROHRABACHER. During that time, was it right off the bat when you set down what we're going to do, you said the final chapters were going to different in terms of their peer review?

Dr. FARLAND. We said that the risk characterization chapter would be developed and then it would be subjected to a public comment and a peer review by the SAB.

And our intent was to have the SAB be the peer review of that risk characterization chapter.

Frankly, one has to make a cut as to when you turn something loose to the public, and the decision that we made was to develop the document internally with the help of some outside scientists to use the extensive scientific expertise of Federal scientists and do a broad inside-the-government review of that document and then to send it to the SAB, giving the SAB the benefit of all of the public comment that we had received over 120 days of public comment period.

And the SAB would be the peer reviewer.

Why didn't we have another peer panel convened in between the development of our report, the Federal review and the SAB? In hindsight, the SAB tells us perhaps it would have been better if we had done that.

But that isn't the way that we approached it.

The question as to whether or not we would have been given some——

Mr. ROHRABACHER. So it would have been better, you are conceding it would have been better to actually follow that process and have his outside peer review?

Dr. FARLAND. Personally, Mr. Chairman, I am not positively convinced of that. The SAB suggests that, and I will take their word for it.

My sense is that we might very well have gotten——

Mr. ROHRABACHER. A moment ago I thought you were conceding that point. Excuse me.

Dr. FARLAND. I was only qualifying that to say that I do agree that it may have been better.

Mr. ROHRABACHER. Okay.

Dr. FARLAND. In hindsight.

The problem I——

Mr. ROHRABACHER. What about in the future when you're doing other type reassessments then? Will you be, you won't have to work in hindsight then, you have got your understanding that you have achieved from hindsight now.

Dr. FARLAND. Right.

Mr. ROHRABACHER. Will you be doing that when you reach, the conclusions that you will be including outside peer reviewers in your conclusion as well as the accumulation of the facts?

Dr. FARLAND. I think that, given the controversial nature of this particular topic and given the way that this has played out, I probably would recommend having that type of a peer review.

We certainly are going to have that type of a peer review before we go back to the SAB with our characterization.

So, the answer to that is "yes."

Mr. ROHRABACHER. All right. And the—but your contention is that this is your strategy all along to have an outside—not to have the outside peer review for the final conclusions?

Dr. FARLAND. The outside peer review was the SAB review.

Mr. ROHRABACHER. Okay.

Dr. FARLAND. In other words, they—one of the issues I think that is important here, Mr. Chairman, is that when we do these peer panels, we actually decide who the peer reviewers are going to be, and the SAB process is an independent process.

And we felt that it was important that the last part of the process have a large group of independent scientists involved in the review.

There were a lot of debates through the course of the development of this process as to when and how peer reviews would be done.

We made the decision to rely heavily on the SAB as an independent peer reviewer of our final document.

Mr. ROHRABACHER. Dr. Gough, do you have a question for Dr. Farland?

Dr. GOUGH. Well, yeah, I have a couple of questions.

I was surprised when you said that—I am not surprised that you say you can accommodate the reviewers' comments.

I am surprised when you said they were minor, they were sort of minor, because one of the criticisms of chapter 9 is its reliance on the default assumption of a linearized no-threshold model for carcinogenicity, whereas chapters 1 through 7 develop a great deal of information about receptors.

And at least a majority of the people on the committee would think that the linearized multistage dose-response model is not appropriate for a receptor-mediated toxic event.

And it seems to me that since this is a deviation from longstanding policy within the agency, this is not a minor change.

Mr. ROHRABACHER. Now, the reason why that I had Dr Gough ask that question is because I am sure there are people in the scientific community that understand that question.

[Laughter.]

I don't know how many people on this panel understand it or this committee understand it, but I am sure it's an important question, and we need to make sure that people are on the record on even issues that the committee doesn't understand.

So, Dr. Farland, would you like to——

Dr. GOUGH. I can make an effort to explain it, if I may.

Mr. ROHRABACHER. All right.

Dr. GOUGH. Okay.

Mr. ROHRABACHER. But let's not make it too long because I would like to ask the other panelists.

Dr. GOUGH. Well, I am also hampered. I can only gesture with one arm.

[Laughter.]

Mr. ROHRABACHER. But has someone been twisting your arm?

[Laughter.]

Dr. GOUGH. But for most toxic events, most toxic effects, we think there is a threshold that you—that the human body or an animal can tolerate a certain number of insults without being pushed over into any toxic consequence.

According to the default assumption that EPA uses for carcinogens, there is no threshold, that at high doses there is a high probability of cancer, at lower doses there is a lower probability of cancer, but the probability of cancer does not reach zero until the dose is zero.

And what the people on the committee for the SAB said was that if you consider the biology that is involved in dioxin, it seems inappropriate now to use this model which associates risk, a direct relationship between exposure and risk.

Mr. ROHRABACHER. All right.

Dr. Farland?

Dr. FARLAND. Mr. Chairman, just a couple of comments in response to Dr. Gough.

First of all, my statement was that these were perhaps minor inconsistencies. I said that I didn't think that there were inconsistencies.

I didn't say they were minor comments. And so, in fact, I think some of the comments are significant that we have, and I don't consider them to be minor. So that is just a point of clarification.

The second point. The SAB report suggests that we used a default approach for reaching the decision to use a linear model.

As Dr. Gough said, the EPA's cancer guidelines suggest that in the absence of available information to inform you in terms of how to do that type of modeling, you use a linear model, which is likely not to underestimate the risk, probably does overestimate the risk, but in each case recognizing that the true risk might even be zero.

It's an area of large uncertainty when you apply that type of a default, and that is recognized by the risk assessment community and the toxicology community.

In the case of dioxin, in chapter 8 we developed a whole line of reasoning around why a linear model, not the default model, but a linear model was appropriate for dioxin.

It had to do with the fact that just because it's a receptor-mediated response, there is no reason to believe that the early events will not be linear.

This gets into some heavy chemistry about receptor and ligand interactions, but generally they follow the law of mass action, and that means that that event early in the process will be linear.

What we don't know is what happens after that, before you finally get a cancer. And those may be nonlinear. But until we know how to draw that curve, our assumption is that because of the biology that is available on dioxin and because we are adding to a background of dioxin that we all carry around, and some effects that may very well be under way, an incremental exposure to dioxin should be modeled in a linear way, not using a default, but model it in a linear way.

Mr. ROHRABACHER. Are you analyzing the cost that that type of approach will place on the society?

Dr. FARLAND. Mr. Chairman, that comes into play when we do the regulatory economic analysis for these sorts of things, because one always wants to know how much uncertainty there is around these estimates and whether or not an upper-bound estimate on risk, like a linear model would produce, is the appropriate approach to use, depending on the decision that will be evaluated.

So, again, my concern right now is that we clarify in our report the use of whatever model that we agree with. The SAB——

Mr. ROHRABACHER. Which fits into what Dr. Lucier was saying about breastfeeding, I guess, that the cost, there is a risk, and even though it might be overestimated in analyzing, the benefits for your breastfeeding outweigh those.

Dr. FARLAND. Absolutely. And, in fact, when we released the document, we also remarked that we thought that the report should not be the cause of people changing their diet, even though we did talk about dioxins in food, because the benefits of a healthy diet seem to us at this point to outweigh risks that may be associated with some small amount of dioxin in the diet for the general population.

Mr. ROHRABACHER. But you are admitting that the approach that you are taking could well magnify the risk that is actually—the public is experiencing.

Dr. FARLAND. There is no doubt that that is going to give an upper-bound estimate on risk.

It's not likely the risk is going to be higher. It probably will be lower.

Mr. ROHRABACHER. All right.

Now, Dr. Lucier, you were complimentary of the EPA's reassessment. But yet the other scientists, you heard in my opening statement the quotes from the other scientists who were not.

Are you basically saying that you were in disagreement with those scientists that expressed their concerns?

Dr. LUCIER. There is clearly debate over, as you articulated in your opening comments, Mr. Chairman, about the dioxin issue, and as I stated in my testimony, that regarding dose-response relationships, there is a legitimate debate over the shape of the dose-response curve in the low-dose region now.

We just had a discussion about the significance of that in relation to receptor binding, and I have a few things to add to it. But I won't right at this time.

I may come back later, if I have a chance.

But most of the scientists who comprise the Science Advisory Board, it is my understanding from reading it, were very complimentary about the reevaluation process.

They were especially complimentary about the background chapters which went into it and stating that they were comprehensive, well-written reviews.

The main criticisms came into the risks, and those have already been talked about, the risk characterization chapter.

Now, I think as I said in my testimony, I think the risk characterization did suffer from its need to condense those 2,000 pages of background into a much shorter document, and I think the ongoing review by the Science Advisory Board will help improve the risk characterization chapter.

So, I don't see where my position and that of most scientists are in disagreement.

Mr. ROHRABACHER. But in terms of those who did complain and the complaints that I acknowledged in my opening statement, you, I take it you disagree with those complaints?

Dr. LUCIER. Which complaint in particular, Mr. Chairman?

Mr. ROHRABACHER. Well, let me get my opening statement. We will read to you the—if I can get it back, I will read you the exact quote that they were—while my staff is looking for that, do you have a question for any of the witnesses on the panel?

Dr. LUCIER. Yes. I wanted to make—it's part question and part comment regarding the receptor mechanisms. I will simply add to what Dr. Farland and Dr. Gough have already said, that if the changes in gene expression that are triggered by the Ah-receptor were clearly linked to toxic responses and we could show how they were linked, then the risk assessment would be easy.

A linear model would be fairly accurate.

However, we don't really understand what that link is between receptor binding, changes in gene expression and more complex biological responses.

In fact, my own laboratory has shown that the dose-response relationships for different kinds of responses to dioxin are much different.

And that has been articulated in some of the background chapters and maybe not articulated well enough in the risk characterization chapter.

Mr. ROHRABACHER. Do you have a question about that?

Dr. LUCIER. Yes. I would simply say that receptor modeling doesn't necessarily imply any particular shape to the dose-response curve.

No dose response can be ruled in or out based solely on the knowledge that a response is receptor-mediated.

Mr. ROHRABACHER. Okay. By the way, what I was asking you to comment on in terms of—was the letter to Science magazine a year ago, of the 18 scientists who worked on an early portion of the reassessment which said, and I quote, that the EPA's conclusions "are heavily dependent on many unproved assumptions and untested hypotheses," and also "urge EPA to clearly distinguish regulatory policy from matters of scientific fact."

I take it that you disagree with those 18 scientists?

Dr. LUCIER. Well, the 18 scientists weren't all part of the original process.

Some of them were involved later on. Some of them were, I mean, and a lot of the people who were involved did not sign that letter.

I think it is consistent with the statement that there is legitimate debate in this arena.

Mr. ROHRABACHER. So, if I can push a little bit, you think there is legitimate debate but you agree or disagree with what they stated?

Dr. LUCIER. I agree with the risk characterization that current exposure levels of dioxin are a public health concern.

I would be hard pressed to put a quantity to that level of concern.

I think, as Dr. Farland and others have pointed out that and as I indicated in my testimony, the actual risk that is estimated may be much lower.

This is clearly a conservative estimate. I would be hard pressed to quantitate that level of concern and wouldn't want to do that.

Mr. ROHRABACHER. Okay.

Dr. Jones——

Dr. FARLAND. Mr. Chairman?

Mr. ROHRABACHER. Oh. Sure. Dr. Farland?

Dr. FARLAND. Could I just weigh in on the issue of the science letter? Mr. Roemer introduced the issue of a spin to some of the documents that surround this reassessment, and this was one, I think, that has gotten a fair amount of spin, if you will allow me that.

The letter basically says that these individuals were involved in the information collection process. Many of them were reviewers of drafts of the documents on panels that had been hired by various groups to review drafts that came out.

Several of them were involved in our process.

And the point, the point here that I want to make is that I agree that all risk assessments have these characteristics that they have said, and I agree with their suggestion to the scientific community that the broader scientific community needs to weigh in on these issues.

Many of the people signed that letter because of those two things.

They didn't sign it because it was critical of EPA's report. They signed it because we needed to involve the broader scientific community in these issues.

So, as much as I hate to endorse something that, because of spin has been suggested to be very critical of the report that I worked on, I do think there is some real legitimacy in the points that were made.

Mr. ROHRABACHER. I think that is very well said.

And Dr. Jones, and then I am going to turn to the rest of our committee here, but, Dr. Jones, would you have a question for anyone on the panel or a statement at this point?

Dr. JONES. One of the things that has always been a question in my mind is that in the U.S. we have taken almost a totally independent approach to dealing with dioxin risks.

In every other country that I am aware of, they have adopted a daily intake threshold of 1 to 10 picograms per kilogram per day

and have proceeded in orderly fashion to go out and find those sources of emissions, and usually they are specific sources, which may be contaminating milk or beef or something adjacent to those facilities, inventory those facilities, and gone about the business of reducing emissions from specific sources.

I am really curious as to why we are off on that track and trying to treat dioxins as a zero-threshold pollutant. As you know, in chapter 9, it is heavily implied that we ought to make this a minimization approach and go out and control every conceivable source of dioxins we can find, which is obviously going to be extremely costly and probably misdirected.

Mr. ROHRABACHER. Do you want to address that to Dr. Farland? I guess you do.

Dr. Farland, would you like to answer that?

Dr. FARLAND. Certainly. Just to address the last point that Dr. Jones made, there is nothing in chapter 9 that suggests that we are talking about trying to get rid of every last molecule of dioxin or any of the regulatory issues that are associated with dioxin.

There are no regulatory directions given at all in this document.

The second thing is that the World Health Organization, which actually determined a tolerable daily intake level for many countries who use a World Health Organization recommendation, didn't rely on individual sources, didn't rely on the question of being close to an incinerator or something like that.

They talked about a background level and how close that background level was to where they saw effects in animals.

They said that, given the fact that, in 1988, their assessment was that animal effects occurred at around 1 nanogram per kilogram per day and daily intakes were at about 10 picograms per kilogram per day, there was a 100-fold difference there, that was probably okay. About a factor of 100.

They recognized that infants that were breastfeeding got more, but as Dr. Lucier said, they agreed that there were benefits to breastfeeding. At this time they didn't think that that exceedance of a tolerable daily intake should be problematic, but they would review it if new data came to light.

In fact, what has happened is that new animal data suggest that effects are occurring at lower levels. We know more about different levels of dioxin and exposures in the general population and people on the tail of the distribution of the population, the ones that are more highly exposed.

And so that margin of safety that the WHO talked about has shrunk. It is less than it was in 1988 when they made their statement.

So the WHO is going back and is reevaluating whether or not that level, which is a management level, not a science level, it's a management level, a tolerable daily intake, should be rethought.

Mr. ROHRABACHER. I am going to make sure other members of the committee have a chance to ask. We will come back to that.

I am very interested in this. For example, on the issue about whether the WHO is talking about animal effects and I know some people suggest that animal effects are not necessarily the human effects of dioxin, and when you are basing it on something like that

that those animal effects, how should we then put that into our own decision making process here?

But I know that Ms. McCarthy has something to do, and if Chairman Brown will yield, we would be very happy to proceed.

Ms. McCarthy?

Ms. MCCARTHY. Thank you, Mr. Chairman.

Thank you, Mr. Brown.

Dr. Farland, I wanted to visit with you a little bit about the forthcoming Air Force study on Vietnam vets and their exposure to the spraying of Agent Orange during their service in the war.

Mr. Gough raised this in his testimony, that EPA should examine the findings of this study and therefore compare those studies on humans to your measurements on animals.

I want to ask you about this forthcoming study and any limitations in it that might preclude you from actually making any unambiguous statements with regard to the effects of dioxin on human health.

I am concerned that this study is a sample of men, that it does not deal with any of the intergenerational issues that we have been discussing here this morning, such as breastfeeding, and also that it really not take into consideration, in addition to gender differences, the health effects that might be different from acute exposure to high levels of dioxin versus chronic exposure to low levels of dioxin.

How valuable will this forthcoming Air Force study be to you, and what might be any shortcomings in it that would preclude us finally bringing some resolution to this important issue for our veterans?

Dr. GOUGH. Ms. McCarthy, I think that you have raised a number of the shortcomings that I would have suggested, in your comment. Again, this is adult males, and so we need to deal with the questions of the gender difference and certainly the age difference in response for dioxin.

That is something that needs to be dealt with, and we will have to look for another study to deal with those.

But that having been said, this is a very important study for us. The reason it's important is that these individuals have been followed for a number of years.

Those individuals have given blood for dioxin analysis as well as being subjected to extensive clinical studies to look very carefully for disease, and the Air Force has done a good job in looking for associations between dioxin levels and various end points that they can measure in this particular population.

Granted, they can't measure all of the ones we would like to look for in different ages and in women.

We are working with the Air Force to look at the latest of their clinical evaluations. That has not yet been published.

The evaluation took place in 1992, and it will be available soon in published form, and in fact we'll have some of the manuscripts shortly. I spoke with one of the principal investigators just within this past week about that.

Secondly, I think that it is quite likely that continuing to follow this group will allow to look at the issue of long latency types of effects.

The problem that we will have is over time the dioxin levels drop and we don't know what happens if you have a situation like Saveso, Italy, where you get a very large amount of dioxin at one time and it drops over time, or in the case of some of our veterans there was an exposure over a few-year period.

The levels are not extremely high; levels in these individuals are not hundreds of times higher than you and I have.

They are higher, but they are not that much higher.

So that those kinds of problems will make it difficult. It won't give us all the answers, but it will continue to be a very good study for us to evaluate, and we will work closely with the Air Force on that.

Ms. MCCARTHY. So, the study itself will not resolve many of the uncertainties that exist but will indeed address some of them to your satisfaction, or it will take another ongoing study to finally resolve these uncertainties? Could I have a bottom line here?

Dr. FARLAND. I am not sure that we will ever be able to resolve all of the uncertainties with our Vietnam veterans, unfortunately.

The situation is such that it becomes more and more difficult over time because the dioxins are going away as part of the natural process of clearing, even though that is a short time.

But these studies will be useful to us in our understanding of the impact on biology. There are some effects that we can look at.

Whether those effects are significant is something that will have to be very carefully analyzed in the sense that some of these may be adaptive responses to exposure to dioxin as opposed to something that we would classify specifically as a health effect or an adverse impact or disease.

So we have to sort those sorts of things out. Unfortunately, we will never have a definitive answer on those exposures, I am afraid.

Ms. MCCARTHY. Well, the definitive answer is death, and it occurs every day to the veterans in my district. Some of them suffering from peripheral neuropathy and other herbicide-related diseases, and our government, while we study and study and study, doesn't seem to share those findings in a positive way with the Department of Veterans' Affairs and others that can actually do something to help these veterans. That is my overarching concern in all of this.

I think the studies are necessary, but I really want to see them come to some sort of conclusion where we can actually then proceed to help the veterans who have been exposed and who have these diseases and are suffering.

Dr. FARLAND. Yes. I would agree with you.

Ms. MCCARTHY. Thank you.

Thank you, Mr. Chairman, very much.

Mr. ROHRABACHER. And now former Chairman Brown?

Mr. BROWN. Thank you, Mr. Chairman.

I appreciate the testimony we have heard this morning. It is helped to bring me a little bit more back up to speed on a subject that I haven't dealt with very much in recent years.

Let me ask you one broad question. Looking at the process as a whole for the review of this study and of chapter 9, would it be—or how would you evaluate overall the system? Is it working in a way reasonably close to what the Congress intended? Do we have

a process which has produced a reasonably objective and broad-ranging analysis of the risk involved here? Are there flaws in it? Is there conflicts of interest or other defects that have biased the study? Is there a better way we could go about it? In other words, are we on the right track or the wrong track with the existing risk assessment processes that we are using?

And I would like each of you to comment briefly on it, not too long. Why don't you start out, Dr. Farland, since you've got the most at stake.

[Laughter.]

Dr. FARLAND. Mr. Brown, I think that we are evolving in our ability to do risk assessment and to involve the scientific community more broadly through both peer involvement and peer review.

And so in that sense, I would say that the risk assessment process in bringing the best science to bear on science decisions and then that science into regulatory decisions is working.

We still have some way to go.

The biggest issue, I guess, is that we have to be sure that we don't find ourselves saying that one size process fits all.

The decisions that are made daily at the EPA constitute risk assessments. Some of them turn into these multiyear efforts, like the dioxin assessment.

I won't comment any further on the process that we have used with dioxin other than to say that I hope there won't be too many that will have to go through as many levels of review and working through consensus in the scientific community as we have done with dioxin.

But clearly this is a process that is evolving. It's working, and it's bringing the best science to bear on these decisions.

Mr. BROWN. Working, but not perfect, then?

Mr. FARLAND. I would say that is a good bottom line, sir.

Mr. BROWN. Dr. Gough?

Mr. GOUGH. Well, the system is working, but it's not working—I don't think it's working so well as Dr. Farland indicates.

In particular, as you have heard from this discussion, receptors are at the crux of understanding how dioxin works, and except for Dr. Lucier on one of the earlier chapters and not on the risk characterization chapter, I think somebody pointed out that nobody who wrote the risk characterization chapter was an expert in receptor biology.

Moreover, no one, or very few people, on the Science Advisory Board's review committee was an expert on receptor biology.

So the people who write the studies and the people who review the studies need to be selected with an understanding of where the important issues are going to be.

The second thing that I think that I would like to comment on chapter 9 is that one thing that I would hope EPA walks away with from this is that it has to exercise more discipline in its selection of data.

There are reports in the literature that exist, that exist as abstracts or very short papers with very little documentation and in some cases EPA treated those with the same seriousness as it did published papers that have been well replicated and with a lot more—with a lot more believability to them.

The last thing, and this just goes back to the chairman's comment to me about making ourselves understandable, one of the criticisms from the review committee was that EPA did not do a good job of presenting its explanations and its decision making process. And that, I am sure that will certainly be improved in this second go-round.

Mr. BROWN. Dr. Lucier?

Dr. LUCIER. Yes. Some general comments.

Some related to the dioxin reassessment and some general issues regarding how we go about using more and the best science available in the risk assessment process.

EPA, in their reevaluation, really has, and as I said in my testimony, done an outstanding job in trying to bring all the science they can into the process to deal with all the areas that create uncertainty in risk assessment.

I mean, one of those areas is dose response, how do we go about estimating low-dose human effects from higher dose animal data.

We can only do this by bringing in the best science that is available, not simply selecting a default approach, a linear model or threshold-based model which may not be necessarily based on good science.

It also helps us select the most appropriate experimental system on which to base our human risk. Clearly, we don't want to wait to see adverse findings in humans before do something.

So, if we have an experimental model because of knowledge of mechanism that would be predictive of what would happen in humans, that would help us a lot in terms of improving the risk assessment process.

The other point is sensitive subpopulations. If we know, as Dr. Gough said, that it's a receptor-mediated process, this does tell us something about whether there might be populations that might be unusually sensitive to dioxin's effects or whatever the chemical of interest is.

Because of their genetic predisposition, they may contain a variant of the receptor that may make them more responsive.

They may be especially young and develop in differentiating systems that would be more sensitive. Or there might be gender differences.

Obviously, if something is acting like an environmental hormone, gender differences might be expected.

It would also help us in exposure assessment in terms of picking up early lesions that might be predictive of response.

What I would like to see is, after having said all that, a review of the process that EPA has undertook by all the interested parties and say we all want to use the best science possible in risk assessment, how can we streamline the process so it doesn't take quite so long the next time around?

Mr. BROWN. Dr. Farland, you are going to look at that question, aren't you, after you get all through with this?

Dr. FARLAND. We are going to.

Mr. BROWN. Because it is a very important question.

Dr. FARLAND. We think that is going to be very instructive for us in terms of future assessments.

Mr. BROWN. Dr. Jones?

Dr. JONES. I just have three comments, and I mentioned those in my earlier testimony.

But number one is I think that in the process the peer review process should go along without so much fanfare as it did during this risk assessment where there was a perceived policy being enunciated at the same time that the peer review was going on.

I was more involved with the background and the exposure sections of the report and not the toxicology side. And one of the problems I had is that those particular chapters were not handled in the same manner as the toxicology chapters, they were all done by internal staff with not a lot of outside inputs.

And I think that had that taken place, I think that a lot of the problems with those chapters would have not been discovered by the SAB.

And I think that those are my two main comments.

Mr. BROWN. Yes.

Let me just, would the Chair indulge me to follow up briefly here?

Let me ask, Dr. Farland, how does this assessment or reassessment compare on a scale of 1 to 10 with others that EPA has to do? Is this a major 10 or is it a 5 or is it a 1? Where does it rank?

Dr. FARLAND. Mr. Brown, this is clearly an outlier on the curve.

Mr. BROWN. It's a 15?

[Laughter.]

Dr. FARLAND. Could be.

We have—we have kidded, and I have made the joke in a lot of talks that I have given, that dioxin is not a chemical, it's a career.

Literally, the EPA has been involved since 1980 in ongoing assessment.

Mr. BROWN. Yes.

Dr. FARLAND. The documents that have been produced are all major works for the agency. The science that goes into them represent thousands and thousands of publications out of the scientific literature.

So, there is a tremendous amount of work that is going on on this class of compounds. One, because it is a very exquisite molecular tool.

It produces responses at very, very low levels. And so you can do intricate molecular biology, you can do all sorts of interesting science with it. All of those need to be factored in.

So this is clearly an outlier in terms of our assessment activities.

Mr. BROWN. But by the same token, isn't what you're learning here vital to your ability to assess other kinds of toxicological insults to humans or other organisms?

Dr. FARLAND. Absolutely. And as has been discussed here, this whole issue of trying to do risk assessment on receptor-mediated types of responses, chemicals that are hormone-like or hormone-memtic-type compounds are out there in the environment; they are found in a number of commercial products and so on.

We need to understand how to do risk assessment on receptor-mediated types of responses and what type of biology they invoke. This is a very good example of trying to do just that.

Mr. BROWN. Well, I am hoping, and I am sure the chairman would share this hope, that you are learning a great deal of the

science that is necessary to produce better risk assessments more effectively and cheaper than you have in the past. And you would concur with that, I presume?

Dr. FARLAND. Mr. Brown, one of the things that is a hallmark of this particular assessment that we haven't discussed is the fact that the agency made a concerted effort to develop some of the critical research data that might be needed as we started out on this risk assessment.

Dr. Birnbaum and her colleagues have developed some very important data in their laboratories over the past couple of years for this reassessment.

Dr. Lucier and his colleagues at NIEHS have done a similar type of thing. And this is science being developed, peer reviewed, published, and brought directly into the risk assessment.

And that's the way things ought to happen.

Mr. BROWN. I recall, you will forgive me for mentioning it, 25 years go I used to interrogate EPA witnesses who would say, "We don't know the answer to this question and we need more research," by saying, "Fine, I think you ought to have the more research, but in another 10 years when I ask you the same question, I would think you would have the answer."

Now I think I was naive and I should say, "Another 50 years I think you should have the answers," because these are questions that we were asking 25 years ago and we still don't have the answers to.

Let me ask this one further question, Mr. Chairman.

We, of course, have suffered from not having adequate sample of humans that we could expose and measure the results of exposure to dioxin here, and even the Air Force study, as has been mentioned, is likely to be inadequate from that standpoint.

Would it be useful, or would you comment on whether it would be useful, to have a very large human population that has been extensively exposed and includes both sexes to do this study on, and, if such a population is available, shouldn't we be making an effort to do that study, if there is such a population, of course?

Dr. FARLAND. Mr. Brown, the most highly exposed population that is really diverse in terms of age and sex and so on was the Seveso population.

Mr. BROWN. The which?

Dr. FARLAND. Seveso, Italy, population that was exposed because——

Mr. BROWN. What about the Vietnamese population that was subjected to the Agent Orange spraying over a period of years and included all of the same population?

Dr. FARLAND. Again, those individuals would not have been what we would call very highly exposed. Most of the individuals that have been sampled are shown to be exposed and are higher than average, and they show the profile for an Agent Orange exposure.

But they are not extremely highly exposed individuals, relatively speaking.

Mr. BROWN. Are you making that statement based upon an investigation of the level of exposure of large populations in Vietnam? Or are you hypothecating that?

Dr. FARLAND. I am making the statement based on what I know from the limited number of samples that are available from the Vietnamese population.

Again, I can only go by that, not by a very broad-based discussion.

We have talked about trying to expand the number of individuals that we have sampled in Vietnam, and I think the opportunity may very well be open to us now that was not open to us years ago.

Mr. BROWN. Yes. I am going to ask further, but if you have any information on it, would you describe any efforts being made to establish an agreement with the Vietnamese for a joint study of the population that might have been exposed on this subject?

Dr. FARLAND. I think it's probably worth mentioning here that there was a trip to Vietnam just within the last six months.

Dr. Lucier might describe the work that he and some of the colleagues did there.

Dr. LUCIER. We were asked, the NIEHS, where I work, was asked, to make a determination of what types of studies would be valuable to conduct in Vietnam to help shed some light about what effects, what the human effects are of dioxin because of the situation that you describe.

We went there about six months ago with a multidisciplinary team comprised of physicians, researchers, and are in the process of generating a report which will identify what those opportunities are. Of course, as you might expect, there are a lot of difficulties in doing studies in Vietnam.

We are also in the process of developing an exchange agreement whereby we can train Vietnamese scientists in our laboratories to go back and do some of that work themselves. But a report is now being generated regarding the existence of opportunities, what difficulties would have to be overcome to achieve those, and once we identify something that is an appropriate study, we will try and fund that through our granting mechanism, providing funding is available.

Mr. BROWN. Thank you.

I won't take more time to explore these questions at this point, Mr. Chairman.

Mr. ROHRABACHER. Thank you very much, Mr. Brown.

Mr. BROWN. Would the Chair indicate whether the record might remain open for some written questions?

Mr. ROHRABACHER. The record will remain open for any written questions.

If the panel will please, we will pass them on to the panel, and we would appreciate your answers. Both the answers and the questions will be submitted for the record.

Just as the former chairman brought up this, and Dr. Farland has mentioned the town in Italy, now I understand that that town in Italy that there was a major, some sort of a major explosion and the people were exposed to very high level of dioxins.

Is this part of your reassessment? Do they mention that? And was there—has there been major health repercussions to this?

Dr. FARLAND. Mr. Chairman, the accident took place in 1976. The first studies of cancer 10 years after the accident have been published now.

There may be some indication of cancer there, although it's very uncertain at this time.

Ten years is not a long latency period for cancer. So perhaps the next set of——

Mr. ROHRABACHER. It's coming close to 20 years now.

Dr. FARLAND. Right. But the study that has been done that has actually looked at the population is only for 10 years. The next update will be coming along, and, hopefully, we will get more information.

Mr. ROHRABACHER. Well, at least for the first 10 years, there wasn't any major health repercussions from that inundation with dioxin?

Dr. FARLAND. If there were, it was very uncertain. The clinical studies don't seem to show very much in those first 10 years.

There are a number of reports in the literature that don't show a lot of effects.

Mr. ROHRABACHER. Now, is this part of your reassessment?

Dr. FARLAND. It is.

Mr. ROHRABACHER. Okay. And I am also told that the French Academy of Sciences has issued a report which finds that there have been no fatalities recorded due to dioxin exposure, and the only documented health effects have been some sort of a skin disorder that they've gotten, chloracne or something.

Is this the case?

Dr. FARLAND. I am familiar with the French Academy report. They did refer to chloracne. As Dr. Gough said, that is the one disease that we know of that is related to high doses and that is known to occur in human populations. All of the others have limited information and so, therefore, are uncertain as to whether they occur in human populations.

Mr. ROHRABACHER. All right. So, what we're talking about here is a problem that is being studied.

That's what your reassessment is all about. And it seems to me that we're talking about—and the reassessment is also very aware of the major costs that are involved in this society if indeed we run off with regulatory proposals that could have an impact on our competitiveness and also on the funds that are available in our society to do other things rather than worry about this particular area.

Dr. FARLAND. Our intent would be to give the best science that we can to the decision makers that have to make those difficult decisions.

Mr. ROHRABACHER. Okay.

Mr. BROWN. Mr. Chairman?

Mr. ROHRABACHER. I would yield.

Mr. BROWN. Would you allow me to raise one question, perhaps? And you might like to answer it.

It seems to me that the conclusion that has been expressed by some of the witnesses that better information about the dose-response curve and the degree to which it is receptor-mediated would result in lower risk assessments; that is, it would give us a lower boundary of what the risk was.

And yet that is a profoundly important scientific question that requires a considerable amount of research.

It would seem that we should all agree that the funds expended on that kind of research, which would have the inevitable effect of lowering risk assessments and mediating the economic cost of excessive regulation ought to be thoroughly supported.

Mr. ROHRABACHER. I would be—I am in total agreement with the distinguished former chairman on that point. I think where my stress is is that when you're dealing with funding research, that is a worthy goal, especially in areas like this where there may, especially when you're talking about Vietnam, where people were exposed, where there may be some risk to the population, and the research is absolutely justified in that expenditure of money..

But before there is something is proven to be a health risk, passing regulations that will cost billions of dollars to the American people, is not justified.

And what we are looking for is to make sure, and in this process of determining risk and what health risks are to the American people, that the regulations do not precede the determination of what that risk is and precede the science.

If the science proves that there is a problem, yes, we will spend those billions of dollars that the regulations will cost, and it will cost—it will cost billions, if not hundreds of billions, of dollars to try to regulate dioxin out of our system.

And that may be what we're going to do, but let's make sure that the science indicates that that expenditure is necessary, because those hundreds of billions of dollars are coming right out of other—of education, of other kinds of health care and of other things that are important to our society.

So, I agree with you that the expenditure on that research is—and your idea about Vietnam, I think, is very well taken.

Mr. BROWN. May I respond briefly, Mr. Chairman?

Mr. ROHRABACHER. Yes, sir.

Mr. BROWN. I happen to agree with you that we do need, of course, to make sure that our regulations are based upon reasonable science.

I don't think there is any disagreement with that.

I would point out, however, that some of the cases in which the greatest hardship has occurred on industry and on the public has been from failure to regulate, at least in the eyes of some, and I cite the example of the chemical Alar, which was criticized for not being regulated, falsely, in my opinion, but the problem there was both lack of regulation and lack of science which would have allowed us to adequately respond to that situation.

Mr. ROHRABACHER. I think the former chairman makes a good point, in the sense that if the government isn't doing its job, panic in the public can actually be a cost as well.

And, Mr. Gough, do you have a comment on that?

Dr. GOUGH. Yes.

Well, I have—you said you would get back to us, and I am going to take advantage to just make a couple of statements.

Mr. ROHRABACHER. All right.

Dr. GOUGH. One is, the Ranch Hands, the Air Force study of the men who were exposed in Vietnam, those men were exposed to 10 to 100, depending on how you calculate it, were exposed to 10 to 100 times the amount of dioxin that most of us are exposed to.

That is exactly the range of exposure that EPA says may cause adverse human health effects.

It's a terribly important study. It does not involve women, it does not involve very young people, and it doesn't involve very old people.

But it is a terribly important study, and I am glad that Dr. Farland acknowledged that, because in the draft that we saw in May, there was no mention of the Ranch Hand study as saying this did not occur, this did not occur, this did not occur.

The EPA simply went through and picked out the three things that were elevated and said this shows that dioxin causes these things.

The second thing I wanted to comment on——

Mr. ROHRABACHER. Excuse me. Could you repeat that?

Dr. GOUGH. Yes. There was an earlier report from the Ranch Hand study.

Mr. ROHRABACHER. Right. The whole point. The last point that you made.

Dr. GOUGH. That instead of EPA presenting a very balanced review of the Ranch Hand study, they had gone through and picked out the three—three end points which might have been elevated as a response to exposure dioxin and had not said a word about all of the other end points which were completely normal.

Mr. ROHRABACHER. Let's have Dr. Farland answer that.

Dr. FARLAND. In chapter 7, which is the human noncancer epidemiology chapter, there is an extensive discussion and review of the Ranch Hand data, and discussion of the range of clinical evaluation that was done and the fact that a number of those are showing nonpositive response, no response that seems to be associated with it.

Mr. ROHRABACHER. Dr. Gough is suggesting that you have underscored those few areas in which there was a negative response or a certain type of response but ignoring the other areas that would say that the people did not have some sort of problem caused by their exposure.

Dr. FARLAND. Well, the issue that we're trying to address here is whether or not there are some effects being seen in human populations within a factor of 10 to 100.

We are quite convinced that there are lots of things that are not occurring because of dioxin.

But there are a few things that appear to be occurring, and those are the ones that are highlighted in the characterization chapter.

The fact that there are changes in testosterone levels in some of these men, the fact that there is a change in glucose tolerance and diabetes incidence in some of those men, and some other clinical manifestations needs to be very carefully looked at because this is a low-level exposure.

Mr. ROHRABACHER. Dr. Gough, is it your point that the report did not go state what isn't happening?

Dr. GOUGH. Yes, because——

Mr. ROHRABACHER. Is that what you're saying?

Dr. GOUGH. If EPA makes a prediction, as it did, that adverse effects to the immune system and several other systems are occurring in exposures 10 to 100 times above background and there is

a population of human beings who have been exposed to that level and those end points are not elevated, it needs to be mentioned. And it was not mentioned in the risk characterization chapter, in chapter 9.

The second thing is I am glad that Dr. Farland clarified the fact that they are not using the default assumption to derive the linear risk model.

On the other hand, I think this exhibits an incredible bias. This is me talking now, this is not the committee. As Dr. Lucier said, we—and as Dr. Farland said—we don't know what happens after the initial binding of dioxin to the receptor.

Most people regard the idea that it's a linear response to be very, very improbable; not impossible, we don't know yet. But it's very, very improbable.

Yet, EPA is using a linear model which it says exaggerates and overestimates the cancer risk. I think that at the very least, and the Science Advisory Board review committee said too, that they should consider other models. And granted, it's hard.

It's difficult. But it's not fair just to take just one and say this is the best we can do.

Mr. ROHRABACHER. Well, we should let Dr. Farland answer that.

Dr. FARLAND. Just briefly, and then Dr. Lucier may also have a——

Mr. ROHRABACHER. You both have about 2 minutes, and then I've got to run.

Dr. FARLAND. Okay. I do think that it is important that we deal with this issue of the dose-response curve and the early events and their connection to frank disease.

I mean, that is really the issue that we are dealing with here.

We looked at the early events and asked whether or not they were linear, and they appear to be. We don't know about some of the other events, but the slope of the curve is about the same as the curves that we get out of the animal studies where we actually measure cancer.

Again, there is uncertainty.

We will use additional models. We will look at the alternatives and write that into the characterization.

The suggestion of the SAB will be—will be taken.

Mr. ROHRABACHER. Dr. Lucier?

Dr. LUCIER. Yes. If I could just say something quickly about that.

Those early events that everyone are talking about really have to be added onto what our current background level is.

We are all exposed to a certain level of dioxin and will have it for our lifetimes. And it looks like those early events are, in fact, linear down to the level that people are exposed to from day-to-day living, and that includes data from experimental systems and also data from human samples from people who have been exposed to dioxin.

So that there is a good body of evidence to support that.

The difficulty, again, and I will reiterate it, is to make that link between those changes in gene expression and what might be termed an adverse health effect.

But it's very, very likely that some responses at the biochemical or molecular level are occurring at exposure levels that are encountered from day-to-day living.

Mr. ROHRABACHER. Are you gentlemen available to come back in one-half hour? Are you all available as a panel? It would be at 1:00.

If you are available, what I would like to do, because I have to go for a vote, and I would like to reconvene this committee hearing at 1:00 and give you all a couple of minutes to just state your summary of what you think you have heard today.

And if you could, for the record.

Now, if you could come back, we will do that at 1:00, and you can maybe grab a sandwich in the meantime, and then we will hear Admiral Zumwalt.

So, with that, the committee is in recess till 1:00.

[Brief recess.]

Mr. ROHRABACHER. The subcommittee will come to order.

I am going to suggest that our panelists each give a 2-minute, if you can keep it to 2 minutes, summary of some of the things that you think came out in today's hearing and just comments that you would like to make in general, summarizing what your particular point that you think is the most important one to come out of the hearing.

I would like to—I don't believe that anyone here will really answer the question that the chairman first posed, the first question that I posed to the hearing today, which was. Did I strive or did I strove?

[Laughter.]

You know, I actually asked several people whether or not I strove to do this or I strived to do this, and I have been getting different answers all the way through the Congress today as to what is the proper English.

Maybe I should ask a member of the press as to whether it is I strived? Is it "I strived" or "I strove" to do that? What is it? Okay.

[Laughter.]

Well, we will have to depend on the judgment of the distinguished former chairman.

Mr. Chairman, do you have an opinion on whether "I strove to do this" or "I strived to do this"?

Mr. BROWN. It's a matter of choice.

Mr. ROHRABACHER. It's a matter of choice.

[Laughter.]

Mr. BROWN. It's what we call a Solomon-like choice.

[Laughter.]

Mr. ROHRABACHER. Thank you.

With that, Dr. Farland, would you like to proceed?

Dr. FARLAND. Mr. Chairman, I think that the discussion this morning has been very useful in trying to bring out some of the issues associated with the difficulty of analyzing the very broad base of information, some of which is newly emerging and that uses new types of techniques, and all of us need to continue to look at how we bring these data to bear and allow the risk assessment process to evolve to the point where it can actually make use of this information. That is one of the critical points here.

We have got to keep the risk assessment process evolving so it can use the new science as it emerges.

That having been said, I guess——

Mr. ROHRABACHER. Excuse me, Dr. Farland. What we will do is we will let you say that, and then we will give you the very last word as well, because you are on the hot seat today and that's the only fair thing to do. Thank you

Dr. FARLAND. Okay.

Mr. ROHRABACHER. Dr. Gough?

Dr. GOUGH. I am going to reiterate two things I said just before we broke.

One is, I think the Ranch Hand study is going to provide a great deal of information about men exposed to the levels that EPA is concerned about.

I am delighted to hear that they are going to consider it seriously.

I was also very happy to hear that they are going to consider alternatives to the linearized model that they used in the last draft of the risk assessment report.

And then—the two things I would like to—the last comment I have is that science is characterized, good science, is characterized by very sharp hypotheses, very sharp statements of what we think is true, and then the designing of studies to find out if the reality agrees with what we think is true.

The looseness, I mean risk assessment in science, you can't hold it to the same criteria, but I think the looseness of the conclusions that I read from the EPA document where we don't know—we don't know what's going to happen, we don't know at what level it's going to happen, but we're sure that it's happening at a lower level than we used to think.

That sort of looseness and vagueness doesn't help anybody, it doesn't provide direction for research, and it certainly won't provide direction for decision makers.

Mr. ROHRABACHER. Dr. Lucier?

Dr. LUCIER. Yes. Just a few comments.

One, I think that we need to, whenever we have activities such as this, is to use all the information that's available, and I think EPA has tried to do this, information on mechanism of action, what happens in experimental models, what happens in humans when they have been exposed accidentally or occupationally to these chemicals such as dioxin, and to put it together in a reasonable balance.

Clearly, we are going to have, in most cases, more information at the animal level rather than the human level. I think fortunately in this case the animal models are going to be very useful coupled with information on human responses to help determine the risk of dioxin.

I would like to see in the risk characterization chapter a sharper definition of what we know and what we don't know. We know a lot of things, there are a lot of things we don't know, and I think that that needs to be articulated, and I think the document is evolving in that way as it goes through the Science Advisory Board process.

Finally, I think EPA has brought the best science possible into the process, and is continuing to do so as it is evolving now.

Mr. ROHRABACHER. Thank you very much, Doctor.

Dr. Jones?

Dr. JONES. I had a third point that I wanted to make in response to Congressman Brown's question earlier, and it went over my own head. That was the issue of promoting regulations to control dioxins from emissions sources before the reassessment process was completed.

And a very, very good example that I raised was the fact that they had overestimated the emissions of dioxins from hospital incinerators by a factor of 10 to 50 to 10-50. And as a result of that, EPA was proceeding to establish emission limitations which essentially would cost the medical service industry somewhere between $2 billion and $4 billion to retrofit incinerators when, in fact, these incinerators probably have very little exposure capacity.

The other point I just wanted to close with is that we have talked about the methodology that EPA should be using with respect to dioxins and how it will apply to other pollutants.

And I am afraid there is another example that will come before you before not too long involving mercury exposure, where EPA has preempted the available science to suggest that mercury is a major problem in our society when, in fact, there is a human study done at human exposure levels which probably will show just the opposite.

So I am not so sure maybe Dr. Farland can respond to that. But it's my understanding that EPA disinvited any comments on their report to Congress, on the peer review on the report to Congress on mercury. Thank you.

Mr. ROHRABACHER. Dr. Farland, please feel free to have 2 minutes' worth of comment and whatever you would to say.

Dr. FARLAND. Well, I guess I can't let the last comment go unaddressed. We do have a report coming up to Congress on mercury. It was extensively peer reviewed. The peer reviews were held in open meetings last winter, and I think you'll find that that represents a very good state-of-the-art assessment of the hazards of mercury. They are based on human studies, and so I will just stop with that.

As far as this particular hearing goes, my sense here is that there is still some confusion about what the Science Advisory Board has said to EPA about their report, and I commend the report that you've received from the Science Advisory Board to your reading. I think it does show a good balance between some very significant recommendations that have been made to improve on the science in the report and some complementary language that does show that more than 80 percent of the report they have no need to see again.

So, that is certainly worthwhile.

The last point that I will make is that there have been a number of studies which have emerged since we finished this report and since the Science Advisory Board met that seemed to be continuing to show effects in human populations at relatively low levels of exposure.

Those will be extremely important for the revision to our report. These include effects in neonates, effects on the nervous system and the immune system.

They are some follow-ups to cancer studies that show additional cancer incidence in human populations exposed to higher levels of exposure. This is in occupational settings.

These will be extremely important to us so that we'll try and bring in the latest information in the next drafts.

Mr. ROHRABACHER. Okay. Thank you very much, Dr. Farland.

Finally, let me say that I made it clear earlier on that we have jurisdiction basically on the issue of how the research is being conducted and not the final issue as to whether or not dioxin poses a major threat and what price do we want to counter that threat.

I would say this, that we have seen in the past where people have done reassessments and people have done studies. For example, I remember there was a major study that cost millions and millions of dollars and maybe even a hundred million dollars, about acid rain, and it was conducted by some of the most prestigious scientists in the United States, and it came out and then it was ignored.

It was laid on the table, it basically—but it basically played down the threat of acid rain and suggested that it had been overblown and that it was not—that acid rain was not the problem that trendy scientists and trendy commentators and trendy politicians portrayed it as.

I would hope that any time that the government does a study and any time that we look into these matters, especially things dealing with health, that we come up with something that is clear, something that is not nebulous, where you make clear statements that will then give us, the policymakers, something on which to make our judgments and that also that we that were making policy judgments do not ignore the science that has been brought forth in these reports.

So, Dr. Farland, I especially want to thank you because I know that you were the one on the hot seat, and I appreciate the fact of your openness today and the way you have conducted yourself.

I want to thank the other panelists as well. We appreciate your opinions, and we appreciate you being here, and I think you have given us a lot of food for thought. So, thank you very much.

Mr. ROHRABACHER. The next panel will be composed of Admiral Zumwalt.

I know you have some very strong feelings on the issue of dioxin. We are very happy to make this forum available to you, and if you would like to proceed and we will just certainly whatever time you need and then we will and then we will follow up with some questions after that.

Thank you very much, Admiral.

If I could ask our friends and staff members and others, Admiral Zumwalt is here, and I think that he deserves the courtesy of being listened to.

Thank you.

STATEMENT OF ADMIRAL ELMO E.R. ZUMWALT, JR., UNITED STATES NAVY [RETIRED], AGENT ORANGE COALITION, ARLINGTON, VA

Admiral ZUMWALT. Thank you, Mr. Chairman and Members of the Committee.

Mr. ROHRABACHER. Admiral, could you turn on your mike and pull your mike a little closer, please?

Admiral ZUMWALT. Can you hear me now?

Mr. ROHRABACHER. Yes, sir.

Admiral ZUMWALT. My statement will deal primarily with EPA's risk assessment process.

In 1989 Secretary of Veterans' Affairs Edward Derwinski asked me to do an analysis for him of the Agent Orange issue. In 1990 I submitted a report listing numerous health effects which, in the judgment of my scientific advisors, were as likely as not to result from exposure of Vietnam veterans to Agent Orange and its dioxin contaminant.

This report commented, first, on the flawed nature of the scientific analyses done by the statutory committee advising the Secretary of Veterans' Affairs, whose deliberations had been heavily weighted by those of its members who had associations with corporations whose production generated dioxin.

Second, that it had been the policy of the U.S. Government in the early '80s to instruct government agencies that it would be most unfortunate if a correlation between Agent Orange and health effects were to be found.

Soon thereafter, the House Committee on Government Operations, on August 9 of 1990, submitted its 12th report, entitled "The Agent Orange Coverup. A Case of Flawed Science and Political Manipulation," which constituted the devastating indictment of the U.S. Government's interference with science.

I quote two of the findings from that report:

"The White House compromised the independence of the CDC and undermined the study by controlling crucial decisions in guiding the course of research at the time it had secretly taken a legal position to resist demands to compensate victims of Agent Orange exposure and industrial accidents."

"The Federal Government has suppressed or minimized findings of ill-health effects among veterans that could be linked to Agent Orange exposure."

My report stated that respected nonindustry scientists concluded there were 28 diseases which met the statutory test that exposure to Agent Orange caused them.

President Bush overruled the Bureau of the Budget, as a result of which the first three diseases were approved as diseases for which the Vietnam veterans or their families should receive compensation, finally, after 15 years of industry manipulation.

Congress reassigned the responsibility for Agent Orange studies to the National Academy of Sciences, which contracted with the Institute of Medicine, IOM, to produce such studies.

Dr. Kenneth Shine, IOM president, established the policy that no scientists would be on the panel who had taken a position pro or con on the correlation between exposure to Agent Orange and health effects.

In July of 1993 the IOM panel issued its first report, as a result of which seven more diseases have been authorized for compensation.

Thus, in the case of the study of dioxin done by IOM to get objective conclusions, the elimination of scientists who had corporate conflicts has led to a total of 10 diseases being found associated with exposure to dioxin.

It is a source of deep concern that the Science Advisory Board reviewing EPA's draft reassessment of dioxin has not been selected on the same basis as the IOM panel but rather contains members and consultants, scientists who have accepted in one form or another financial support from corporations who have a strong interest in finding negative correlation between dioxin and health effects.

The Science Advisory Board review of EPA dioxin reassessment has thus been tilted in some respects away from proper scientific conclusions for the purpose of making the findings of EPA less than objective in places for the benefit of interested corporations.

In summary, regarding the reassessment process, the EPA, without the manipulation of company docs, came up with scientifically objective results. The SAB, with company doc members, denigrated and manipulated EPA's outcome.

Notwithstanding that, objective scientists have peer reviewed the significant portion of EPA's work in the study by Drs. DeVito, Birnbaum, Farland, and Gastowitz in the publication "Environmental Health Perspective."

The process that IOM has used, using only scientists who have no conflicts, has resulted in a situation where one Cabinet department, VA, recognizes the harmful effects of exposure to dioxin in the case of 10 diseases.

I strongly urge Congress enact a requirement that future membership of the Science Advisory Board contain no scientists whose research or livelihood in main or in part is dependent upon financial support from corporations.

Vietnam veterans have been denied for over 20 years the benefits which the law would have provided had scientific truth prevailed over pseudo-scientific manipulation.

Surely it is not too much to ask that the financial conflicts of interest of the members and consultants of the Science Advisory Board and of today's industry witnesses be published within the final record of the hearing.

Thank you, Mr. Chairman.

[The prepared statement and attachments of Admiral Zumalt follow:]

E. R. ZUMWALT, JR.
ADMIRAL, U. S. NAVY (RET.)

STATEMENT BY
Admiral E. R. Zumwalt, Jr., USN (Ret.)
Chairman, Agent Orange Coordinating Council

before the

House Subcommittee on Energy and Environment

December 13, 1995

I am here in my capacity as Chairman of the Agent Orange Coordinating Council whose membership consists of most of the veterans and veteran-related organizations. I became involved in great detail in the Agent Orange issue in the following manner.

I commanded U.S. Naval Forces, Vietnam, from 1968 until 1970 and had further responsibilities for forces fighting in Vietnam while I served a member of the Joint Chiefs of Staff from 1970 to 1974.

In 1989 the Secretary of Veterans Affairs, The Honorable Edward Derwinski, asked me to serve as an unpaid special assistant to do an analysis for him of the Agent Orange issue. I spent seven months, in conjunction with respected scientists, reviewing the studies on dioxin. In May 1990, I submitted a report which listed numerous health effects which, in my judgement and that of my scientific advisors, were as likely as not to result from exposure of Vietnam veterans to Agent Orange and its dioxin contaminant.

This report, among other things, commented on the flawed nature of the scientific analyses done by the statutory committee advising the Secretary of Veterans Affairs, the Committee on Environmental Health Hazards, whose deliberations had, in my opinion, been heavily weighted by those of its members who had associations with corporations whose products generated dioxin.

In addition, I was able to establish that it had been the policy of the U.S. Government in the early `80s to instruct government agencies involved in Agent Orange studies that it would be most unfortunate if a correlation between Agent Orange and health effects were to be found.

A copy of my report to Secretary Derwinski is attached.

Soon thereafter, the House Committee on Government Operations

on August 9, 1990, submitted its 12th report entitled *The Agent Orange Coverup: A Case of Flawed Science and Political Manipulation*, copy attached, which, in my judgement, constituted a devastating indictment of the U.S. Government's interference with science.

I quote two of the findings of that report:

"The White House compromised the independence of the CDC and undermined the study by controlling crucial decisions and guiding the course of research at the same time it had secretly taken a legal position to resist demands to compensate victims of Agent Orange exposure and industrial accidents."

"The Federal Government has suppressed or minimized findings of ill health effects among Vietnam veterans that could be linked to Agent Orange exposure."

I should note that industry weighed in by insuring that a minority of the committee took issue with the findings concerning the interference of the government with science.

My report stated that based on my review with respected scientists of all available studies, there were 28 diseases which met the statutory test that it was "as likely as not" that exposure to Agent Orange caused them. At about the same time, the Agent Orange Scientific Task Force, commissioned by veterans organizations to study the issue, found that a large number of diseases were as likely as not a result of exposure to Agent Orange.

To his credit, President Bush on being apprised of the foregoing overruled the Bureau of the Budget and accepted Secretary Derwinski's recommendations, as a result of which three diseases: chloracne, soft tissue sarcoma, and non-Hodgkin lymphoma were approved as diseases for which Vietnam veterans or their families should receive compensation.

Soon after the foregoing events, Congress disestablished the Committee on Environmental Health Hazards and assigned the responsibility for Agent Orange studies to the National Academy of Sciences which contracted with the Institute of Medicine (IOM) to produce such studies.

Dr. Kenneth Shine, President of the Institute of Medicine, agreed to establish the policy that no scientists would be on the panel who had taken a position pro or con on the correlation between exposure to Agent Orange and health effects. Highly credible scientists who had not previously taken such positions were named to a panel which reviewed all the literature. In July

of 1993, the IOM panel issued its first report as a result of which seven more diseases have been authorized for compensation.

Thus in the case of the study of dioxin done by IOM to get to objective conclusions for veterans exposed to Agent Orange, the elimination of scientists who had corporate conflicts has led to a total of ten diseases being found, as likely as not, associated with such exposure.

It is a source of deep concern that the Science Advisory Board reviewing EPA's draft reassessment of dioxin has not been selected on the same basis as the IOM panel, but rather contains as members and consultants scientists who have accepted in one form or another financial support from corporations who have a strong interest in finding negative correlation between dioxin and health effects.

In my judgement, based on consultation with scientists for whom I have great respect, the Science Advisory Board review of EPA dioxin reassessment, is, like the work of the flawed Committee on Environmental Health Hazards, tilted in some respects away from proper scientific conclusions, for the purpose of making the findings of EPA less than objective in places, for the benefit of interested corporations.

I regret that the practice of inviting scientists with obvious conflicts of interest to testify is being continued by this committee.

I strongly urge that your committee cause Congress to enact by statute a requirement that future membership of the Science Advisory Board contain no scientists whose research or livelihood, in main or in part, is dependent upon financial support from corporations. We have learned that such scientists can be less than objective. The result is that Vietnam veterans have been denied for over 20 years the benefits which the law would have provided had scientific truth prevailed over pseudo-scientific manipulation.

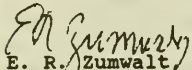
With regard to the present hearing, surely it is not too much to ask that the financial conflicts of interest of the members and consultants of the Scientific Advisory Board be published within the final record of the hearing.

With regard to the substantive outcome of these hearings, I am aware of the great pressures brought to bear by lobbyists for the corporations who produce dioxin as a by-product of the operations. As a representative of the major veterans groups by virtue of my chairmanship of their Agent Orange Coordinating Council, I am also aware that thousands of Vietnam veterans and their families are equally convinced that corporate and government manipulation of science has delayed for years their obtaining appropriate compensation for the diseases resulting from exposure to Agent

Orange. By and large such veterans have supported the efforts that I have made to initiate joint research of Agent Orange using the heavily exposed Vietnamese people to obtain further evidence of health effects. The veterans, by and large, have recognized that the time has come to put the war behind us with the restoration of diplomatic relations with the former enemy regime. They clamor for the final step in such closure to take place. That final step is to establish the scientific truth with regard to their exposure to Agent Orange.

This hearing, if it does not interfere with the objective scientific analysis carried out by EPA in its draft dioxin risk reassessment, will have contributed to the achievement of that final step.

Sincerely,



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Enclosures

REPORT TO THE SECRETARY OF THE DEPARTMENT OF VETERANS AFFAIRS ON THE ASSOCIATION BETWEEN ADVERSE HEALTH EFFECTS AND EXPOSURE TO AGENT ORANGE

As Reported by Special Assistant
Admiral E.R. Zumwalt, Jr.

May 5, 1990

I. INTRODUCTION

On October 6, 1989 I was appointed as special assistant to Secretary Derwinski of the Department of Veterans Affairs to assist the Secretary in determining whether it is at least as likely as not that there is a statistical association between exposure to Agent Orange and a specific adverse health effect.

As special assistant, I was entrusted with evaluating the numerous data relevant to the statistical association between exposure to Agent Orange and the specific adverse health effects manifested by veterans who saw active duty in Vietnam. Such evaluations were made in accordance with the standards set forth in Public Law 98-542, the Veterans' Dioxin and Radiation Exposure Compensation Standards Act and 38 C.F.R. § 1.17, regulations of the Department of Veterans Affairs concerning the evaluation of studies relating to health effects of dioxin and radiation exposure.

Consistent with my responsibilities as special assistant, I reviewed and evaluated the work of the Scientific Council of the Veterans' Advisory Committee on Environmental Hazards and commissioned independent scientific experts to assist me in evaluating the validity of numerous human and animal studies on the effects of exposure to Agent Orange and/or exposure to herbicides containing 2,3,7,8 tetrachlorodibenzo-para-dioxin (TCDD or dioxin). In addition, I reviewed and evaluated the protocol and standards employed by government sponsored studies

to assess such studies' credibility, fairness and consistency with generally accepted scientific practices.

After reviewing the scientific literature related to the health effects of Vietnam Veterans exposed to Agent Orange as well as other studies concerning the health hazards of civilian exposure to dioxin contaminants, I conclude that there is adequate evidence for the Secretary to reasonably conclude that it is at least as likely as not that there is a relationship between exposure to Agent Orange and the following health problems: non-Hodgkin's lymphoma, chloracne and other skin disorders, lip cancer, bone cancer, soft tissue sarcoma, birth defects, skin cancer, porphyria cutanea tarda and other liver disorders, Hodgkin's disease, hematopoietic diseases, multiple myeloma, neurological defects, auto-immune diseases and disorders, leukemia, lung cancer, kidney cancer, malignant melanoma, pancreatic cancer, stomach cancer, colon cancer, nasal/pharyngeal/esophageal cancers, prostate cancer, testicular cancer, liver cancer, brain cancer, psychosocial effects and gastrointestinal diseases.

I further conclude that the Veterans' Advisory Committee on Environmental Hazards has not acted with impartiality in its review and assessment of the scientific evidence related to the association of adverse health effects and exposure to Agent Orange.

In addition to providing evidence in support of the conclusions stated above, this report provides the Secretary with

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a review of the scientific, political and legal efforts that have occurred over the last decade to establish that Vietnam Veterans who have been exposed to Agent Orange are in fact entitled to compensation for various illnesses as service-related injuries.

II. AGENT ORANGE USAGE IN VIETNAM

Agent Orange was a 50:50 mixture of 2,4-D and 2,4,5-T. The latter component, 2,4,5-T, was found to contain the contaminant TCDD or 2,3,7,8-tetrachlorodibenzo-para-dioxin (i.e. dioxin), which is regarded as one of the most toxic chemicals known to man.[1]

From 1962 to 1971 the United States military sprayed the herbicide Agent Orange to accomplish the following objectives: 1)

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[1] See CDC Protocol for Epidemiologic Studies on the Health of Vietnam Veterans (November, 1983), p. 4 (The CDC Protocol also contains a literature review as of 1983 of the health effects on animals and humans exposed to herbicides and dioxin, pp. 63-78. The literature review documents health problems such as chloracne, immunological suppression, neurological and psychological effects, reproductive problems such as birth defects, carcinogenic effects such as soft tissue sarcomas, lymphomas and thyroid tumors, and various gastrointestinal disorders) ; See also General Accounting Office, "Report by the Comptroller General: Health Effects of Exposure to Herbicide Orange in South Vietnam Should Be Resolved," GAO-CED-79-22 at 2 (April 6, 1979) [hereinafter GAO Report, 1979].

Dioxin is a family of chemicals (75 in all) that does not occur naturally, nor is it intentionally manufactured by any industry. The most toxic dioxin is called 2,3,7,8 - TCDD. Dioxins are produced as byproducts of the manufacture of some herbicides (for example, 2,4,5-T), wood preservatives made from trichlorophenals, and some germicides. Dioxins are also produced by the manufacture of pulp and paper, by the combustion of wood in the presence of chlorine, by fires involving chlorinated benzenes and biphenyls (e.g. PCBs), by the exhaust of automobiles burning leaded fuel, and by municipal solid waste incinerators.

defoliate jungle terrain to improve observation and prevent enemy ambush; 2) destroy food crops; and 3) clear vegetation around military installations, landing zones, fire base camps, and trails.[2]

Unlike civilian applications of the components contained in Agent Orange which are diluted in oil and water, Agent Orange was sprayed undiluted in Vietnam. Military applications were sprayed at the rate of approximately 3 gallons per acre and contained approximately 12 pounds of 2,4-D and 13.8 pounds of 2,4,5-T.[3]

Although the military dispensed Agent Orange in concentrations 6 to 25 times the manufacturer's suggested rate, "at that time the Department of Defense (DOD) did not consider herbicide orange toxic or dangerous to humans and took few precautions to prevent exposure to it."[4] Yet, evidence readily suggests that at the time of its use experts knew that Agent Orange was harmful to military personnel.[5]

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[2] See Bruce Myers, "Soldier of Orange: The Administrative, Diplomatic, Legislative and Litigatory Impact of Herbicide Agent Orange in South Vietnam," 8 B. C. Env't. Aff. L. Rev. 159, 162 (1979).

[3] See GAO Report, 1979 at 2, 3 n.1; See also Myers, 8 B.C. Env't Aff. L. Rev. at 162. In contrast, civilian applications of 2,4,5-T varied from 1 to 4 pounds per acre.

[4] General Accounting Office, "Ground Troops in South Vietnam Were in Areas Sprayed with Herbicide Orange," FPCD 80-23, p.1 (November 16, 1979).

[5] Letter from Dr. James R. Clary to Senator Tom Daschle (September 9, 1988). Dr. Clary is a former government scientist with the Chemical Weapons Branch, BW/CW Division, Air Force Armament Development Laboratory, Eglin AFB, Florida. Dr. Clary was instrumental in designing the specifications for the A/A 45y-1 spray tank (ADO 42) and was also the scientist who prepared the

The bulk of Agent Orange herbicides used in Vietnam were reportedly sprayed from "Operation Ranch Hand" fixed wing aircraft. Smaller quantities were applied from helicopters, trucks, riverboats, and by hand. Although voluminous records of Ranch Hand missions are contained in computer records, otherwise known as the HERBS and Service HERBs tapes, a significant, if not major source of exposure for ground forces was from non-recorded, non Ranch Hand operations.[6]

Widespread use of Agent Orange coincided with the massive buildup of U.S. military personnel in Vietnam, reaching a peak in

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final report on Ranch Hand: Herbicide Operations in SEA, July 1979. According to Dr. Clary:

> When we (military scientists) initiated the herbicide program in the 1960's, we were aware of the potential for damage due to dioxin contamination in the herbicide. We were even aware that the 'military' formulation had a higher dioxin concentration than the 'civilian' version due to the lower cost and speed of manufacture. However, because the material was to be used on the 'enemy', none of us were overly concerned. We never considered a scenario in which our own personnel would become contaminated with the herbicide. And, if we had, we would have expected our own government to give assistance to veterans so contaminated.

See also notes 13, 73-75 and accompanying text infra for additional information of the manufacturer's awareness of the toxicity of Agent Orange.

[6] Combat units, such as the "Brown Water Navy," frequently conducted "unofficial" sprayings of Agent Orange obtained from out of channel, and thus unrecorded sources. Additionally, as Commander, U.S. Naval Forces, Vietnam, I was aware that Agent Orange issued to Allied forces was frequently used on unrecorded missions.

1969 and eventually stopping in 1971.[7] Thus, according to an official of the then Veterans Administration, it was "theoretically possible that about 4.2 million American soldiers could have made transient or significant contact with the herbicides because of [the Ranch Hand Operation]." [8]

A. REASONS FOR PHASE OUT

Beginning as early as 1968, scientists, health officials, politicians and the military itself began to express concerns about the potential toxicity of Agent Orange and its contaminant dioxin to humans. For instance, in February 1969 The Bionetics Research Council Committee ("BRC") in a report commissioned by the United States Department of Agriculture found that 2,4,5-T showed a "significant potential to increase birth defects." [9] Within four months after the BRC report, Vietnamese newspapers began reporting significant increases in human birth defects ostensibly due to exposure to Agent Orange.[10]

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[7] GAO Report 1979, supra note 1, at 29. See also note 82 and accompanying text infra for a discussion of the correlation between the spraying of Agent Orange and the hospitalization of Vietnam soldiers for disease and non-battle related injuries.

[8] House Comm. on Veteran's Affairs, 95th Cong., 2d Sess., Herbicide "Agent Orange", Hearings before the Subcommittee on Medical Facilities and Benefits, (Oct. 11, 1978) (Statement of Maj. Gen. Garth Dettinger USAF, Deputy Surgeon General USAF at 12).

[9] Myers at 166.

[10] Id. While birth defects did significantly increase in Saigon, critics contend that Saigon was not an area where the preponderance of defoliation missions were flown and argue that such increases were due primarily to the influx of U.S. medical personnel who kept better records of birth defects. Subsequent

By October, 1969, the National Institute of Health confirmed that 2,4,5-T could cause malformations and stillbirths in mice, thereby prompting the Department of Defense to announce a partial curtailment of its Agent Orange spraying.[11]

By April 15, 1970, the public outcry and mounting scientific evidence caused the Surgeon General of the United States to issue a warning that the use of 2,4,5-T might be hazardous to "our health".[12]

On the same day, the Secretaries of Agriculture, Health Education and Welfare, and the Interior, stirred by the publication of studies that indicated 2,4,5-T was a teratogen (i.e. caused birth defects), jointly announced the suspension of its use around lakes, ponds, ditch banks, recreation areas and

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studies in Vietnam confirm the incidence of increased birth defects among civilian populations exposed to Agent Orange. See e.g. Phuong, et. al. "An Estimate of Reproductive Abnormalities in Women Inhabiting Herbicide Sprayed and Non-herbicide Sprayed Areas in the South of Vietnam, 152-1981 18 Chemosphere 843-846 (1989) (significant statistical difference between hydatidiform mole and congenital malformations between populations potentially exposed and not exposed to TCDD); Phuong, et. al., "An Estimate of Differences Among Women Giving Birth to Deformed Babies and Among Those with Hydatidiform Mole Seen at the OB-GYN Hospital of Ho Chi Minh City in the South of Vietnam," 18 Chemosphere 801-803 (1989) (statistically significant connection between frequency of the occurrence of congenital abnormalities and of hydatidiform moles and a history of phenoxyherbicide exposure); Huong, et. al., "An Estimate of the Incidence of birth Defects, Hydatidiform Mole and Fetal Death in Utero Between 1952 and 1985 at the OB-GYN Hospital of Ho Chi Minh City, Republic of Vietnam," 18 Chemosphere 805-810 (1989) (sharp increase in the rate of fetal death in utero, hydatidiform mole (with or without choriocarcinoma) and congenital malformations from the pre 1965-1975 period, suggesting possible association to phenoxyherbicide exposure).

[11] Myers at 167

[12] Id.

homes and crops intended for human consumption.[13] The Department of Defense simultaneously announced its suspension of all uses of Agent Orange.[14]

B. HEALTH STUDIES

As Agent Orange concerns grew, numerous independent studies were conducted between 1974 and 1983 to determine if a link exists between certain cancerous diseases, such as non-Hodgkin's lymphoma and soft-tissue sarcomas, and exposure to the chemical components found in Agent Orange. These studies suggested just such a link.

In 1974, for example, Dr. Lennart Hardell began a study which eventually demonstrated a statistically significant correlation between exposure to pesticides containing dioxin and the development of soft tissue sarcomas.[15]

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[13] Id. Although Dow Chemical Company, the primary manufacturer of 2,4,5-T and 2,4-D, denied this teratogenicity, Dow's own tests confirmed that when dioxin was present in quantities exceeding production specifications, birth defects did occur. See J. McCullough, Herbicides: Environmental Health Effects; Vietnam and the Geneva Protocol; Developments During 1979, 13 (1970) (Congressional Research Report No. UG 447, 70-303SP). Pressure from industry subsequently led to some relaxation of the limits placed on the 2,4,5-T and 2,4-D. The only current uses for these chemicals in the United States are on rice, pastures, rangelands and rights of way.

[14] Id. at 167. See also Dow Chemical v. Ruckelshaus, 477 F. 2d 1317, 1319 (8th Cir. 1973) (secretaries announcement quoted in the opinion).

[15] Hardell, L. and Sandstrom, A. "Case-control Study: Soft Tissue Sarcomas and Exposure to Phenoxyacetic Acids or Chlorophenols," 39 Brit. J. Cancer, 711-717 (1979). See also note 89 infra for the confirming results of follow-up studies by Hardell and others.

In 1974, Axelson and Sundell reported a two-fold increase of cancer in a cohort study of Swedish railway workers exposed to a variety of herbicides containing dioxin contaminants.[16]

By 1976, the Occupational Safety and Health Administration, established rigorous exposure criteria for workers working with 2,4,5-T.[17]

In 1977 the International Agency for Research on Cancer (IARC), while cautioning that the overall data was inconclusive, reported numerous anomalies and increased mortality rates in animals and humans exposed to 2,4-D or 2,4,5-T.[18]

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[16] Axelson and Sundell, "Herbicide Exposure, Mortality and Tumor Incidence: An Epidemiological Investigation on Swedish Railroad Workers," 11 Work Env't. Health 21-28 (1974).

[17] U.S. Occupational Safety and Health Administration (1976), Air Contaminants; U.S. Code, Federal Register 29, Part 1910.93 at p. 27.

[18] With regard to 2,4-D, the IARC found the following anomalies: elevated levels of cancer in rats; acute and short-term oral toxicity in mice, rabbits, guinea pigs and rats--death, stiffness in the extremities, incoordination, stupor, myotonia, and other physical abnormalities; in monkeys, injections caused nausea, vomiting, lethargy, muscular incoordination and head droop, fatty degeneration of the liver, spleen, kidneys and heart; foetal anomaly increases in some species; post-birth death rates increased in some species; higher mortality rates and morphological alterations in pheasant embryos and their chicks when spraying took place under simulated field conditions; higher mortality rates in rat pups in a 3 generation exposure; gene mutation after exposure to high concentrations; chromosomal aberrations when cultured human lymphocytes were exposed; increased frequency of aberrant metaphases (2 to 4 times) in mice exposed to toxic concentrations.

In humans the IARC found that: a 23 year old farming student, a suicide, had 6 grams of 2,4-D in his body, acute congestion of all organs, severe degeneration of ganglion cells in the central nervous system; 3 cases of peripheral neuropathy in humans sprayed with 2,4-D with initial symptoms of nausea, vomiting, diarrhea, swelling and aching of feet and legs with latency, in individual cases, paresthesia in the extremities, pain in the legs, numbness and aching of fingers and toes, swelling in hand joints, flaccid

In 1978, the Environmental Protection Agency issued an emergency suspension of the spraying of 2,4,5-T in national forests after finding "a statistically significant increase in the frequency of miscarriages" among women living near forests sprayed with 2,4,5-T.[19]

In 1980, another provocative mortality study of workers

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parapheresis; similar case reports in agriculture workers sprayed by 2,4-D; workers associated with 2,4-D developed symptoms of somnolence, anorexia, gastralgia, increased salivation, a sweet taste in the mouth, a sensation of drunkenness, heaviness of the legs and hyperacusea, rapid fatigue, headache, loss of appetite, pains in the region of liver and stomach, weakness, vertigo, hypotension, bradycardia, dyspeptic symptoms, gastritis, liver disfunction, changes in metabolic processes.

With regard to 2,4,5-T's effect on animals the IARC found: it can increase the frequency of cleft palates in some strains of mice; fetal growth retardation may also be observed; cystic kidneys were observed in two strains of mice; in purest available form, it induced some fetal effects and skeletal anomalies in rats as well as behavioral abnormalities, changes in thyroid activity and brain serotonin levels in the progeny; increases in intrauterine deaths and in malformations in rats; fetal death and teratogenic effects in Syrian golden hamsters; chromosomal abnormalities.

The IARC reported in 1977 with respect to 2,4,5-T's effects on humans that: workers exposed at a factory in the USSR had skin lesions, acne, liver impairment, and neurasthenic syndrome; similar findings were reported by Jerasneh, et al (1973, 1974) in a factory in Czechoslovakia which in 1965-68 produced 76 cases of chloracne, 2 deaths from bronchogenic cancers. Some workers had porphyria cutanea tarda, urophryimuria, abnormal liver tests, severe neurasthenia, depression syndrome, peripheral neuropathy; in a 1975 accident in West Virginia, 228 people were affected. Symptoms included chloracne, melanosis, muscular aches and pains, fatigue, nervousness, intolerance to cold; 4 workers of 50 affected in a similar accident in the Netherlands in 1963 died within 2 years and at least 10 still had skin complaints 13 years later.

[19] June 1979 Congressional Hearings before House Commerce Committee, Subcommittee on Oversight and Investigations, quoted in "Human Disease Linked to Dioxin: Congress Calls for 2,4,5-T Ban After Dramatic Herbicide Hearings", 28 Bioscience 454 (August 1979). This study, otherwise known as the Alsea Study, has been cited as showing the first correlation between 2,4,5-T (and presumably its TCDD contaminant) and teratogenic effects in humans.

involved in an accident at an industrial plant which manufactured dioxin compounds suggested that exposure to these compounds resulted in excessive deaths from neoplasms of the lymphatic and hematopoietic tissues.[20]

On September 22, 1980, the U.S. Interagency Work Group to Study the Long-term Health Effects of Phenoxy Herbicides and Contaminants concluded "that despite the studies' limitations, they do show a correlation between exposure to phenoxy acid herbicides and an increased risk of developing soft-tissue tumors or malignant lymphomas."[21]

To be sure, there remain skeptics who insist that the studies failed in one respect or another to establish a scientifically acceptable correlation.[22] Yet, it can fairly be said that the general attitude both within and outside the scientific community was, and continues to be increasing concern over the mounting evidence of a connection between certain cancer

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[20] Zack and Suskind, "The Mortality Experience of Workers Exposed to TCDD in a Trichlorophenol Process Accident," 22 Journal of Medicine, 11-14 (1980).

[21] See U.S. Interagency Workgroup to Study the Long-Term Health Effects of Phenoxy Herbicides and Contaminants (September 22, 1980)(executive summary).

[22] See e.g., "The Weight of the Evidence on the Human Carcinogenicity of 2,4-D" (January 1990) (This report, sponsored by the National Association of Wheat Growers Foundation and a grant from the Industry Task Force II on 2,4-D Research Data, an association of manufacturers and commercial formulators of 2,4-D, concluded that the toxicological data on 2,4-D does not provide a strong basis for predicting that 2,4-D is carcinogenic to humans. Nevertheless, the panel reviewing the evidence did conclude that "evidence indicates that it is possible that exposure to 2,4-D can cause cancer in humans.").

illnesses and exposure to dioxins.

III. VETERANS' DIOXIN AND RADIATION EXPOSURE COMPENSATION STANDARDS ACT OF 1984

With the increasing volume of scientific literature giving credence to the belief of many Vietnam Veterans that exposure to Agent Orange during their military service was related to their contraction of several debilitating diseases -- particularly non-Hodgkin's lymphoma, soft tissue sarcoma ("STS")(malignant tumors that form in muscle fat, or fibrous connective tissue) and porphyria cutanea tarda ("PCT")(deficiencies in liver enzymes) -- Vietnam Veterans rightfully sought disability compensation from the Veterans Administration ("VA").

The VA determined, however, that the vast majority of claimants were not entitled to compensation since they did not have service connected illnesses.[23] As a consequence, Congress attempted to alter dramatically the process governing Agent Orange disability claims through passage of the Veterans' Dioxin and Radiation Exposure Compensation Standards Act of 1984

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[23] By October 1, 1983, 9170 veterans filed claims for disabilities that they alleged were caused by exposure to Agent Orange. The VA denied compensation to 7709 claimants on the grounds that the claimed diseases were not service connected. Only one disease was deemed associated with service related exposure to Agent Orange, a skin condition known as chloracne. See House Report No. 98-592, reprinted in U.S.Code Cong. & Adm. News, 98th Cong. 2d Sess.,1984, at 4452. See also Nehmer v. U.S. Veterans Administration, 712 F.Supp. 1404, 1407 (1989).

(hereinafter the "Dioxin Standards Act").[24] To ensure that the VA provided disability compensation to veterans exposed to herbicides containing dioxin while serving in Vietnam,[25] Congress authorized the VA to conduct rulemaking to determine those diseases that were entitled to compensation as a result of a service-related exposure to Agent Orange.[26]

In promulgating such rules, the Dioxin Standards Act required the VA to appoint a Veterans' Advisory Committee on Environmental Hazards (the "Advisory Committee") -- composed of experts in dioxin, experts in epidemiology, and interested members of the public -- to review the scientific literature on dioxin and submit periodic recommendations and evaluations to the Administrator of the VA.[27] Such experts were directed to evaluate the scientific evidence pursuant to regulations promulgated by the VA, and thereafter to submit recommendations

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[24] Veterans' Dioxin and Radiation Exposure Compensation Standards Act, Pub. L. 98-542, Oct. 24, 1984, 98 Stat. 2727 (hereinafter the Dioxin Standards Act). In passing the Act Congress found that Vietnam Veterans were "deeply concerned about possible long term health effects of exposure to herbicides containing dioxin,"(Section 2 (1)), particularly since "[t]here is scientific and medical uncertainty regarding such long-term adverse health effects." (Section 2 (2)). In responding to this uncertainty, Congress mandated that "thorough epidemiological studies of the health effects experienced by veterans in connection with exposure ... to herbicides containing dioxin" be conducted, (Section 2(4)), especially in light of the fact that "[t]here is some evidence that chloracne, porphyria cutanea tarda, and soft tissue sarcoma are associated with exposure to certain levels of dioxin as found in some herbicides." (Section 2 (5)).

[25] Id. at Section 3.

[26] Id. at Section 5.

[27] Id. at Section 6.

and evaluations to the Administrator of the VA on whether "sound scientific or medical evidence" indicated a connection to exposure to Agent Orange and the manifestation of various diseases.[28]

In recognition of the uncertain state of scientific evidence and the inability to make an absolute causal connection between exposure to herbicides containing dioxin and affliction with various rare cancer diseases,[29] Congress mandated that the VA Administrator resolve any doubt in favor of the veteran seeking compensation. As stated in the Dioxin Standards Act:

> It has always been the policy of the Veterans Administration and is the policy of the United States, with respect to individual claims for service connection of diseases and disabilities, that when, after consideration of all the evidence and material of record, there is an approximate balance of positive and negative evidence regarding the merits of an issue material to the determination of a claim, the benefit of the doubt in resolving each such issue shall be given to the claimant.[30]

A. NEHMER V. U.S. VETERANS ADMINISTRATION

Despite Congressional intent to give the veteran the benefit of the doubt, and in direct opposition to the stated purpose of

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[28] Id. at Section 5.

[29] See Nehmer v. U.S. Veterans Admin., 712 F. Supp. 1404, 1418 (N.D. Cal. (1989) wherein the court found after reviewing the legislative history of the Act "that Congress intended service connection to be granted on the basis of 'increased risk of incidence', or a 'significant correlation' between dioxin and various diseases," rather, than on the basis of a causal relationship.

[30] See Dioxin Standards Act at Section 2 (13).

the Dioxin Standards Act to provide disability compensation to Vietnam Veterans suffering with cancer who were exposed to Agent Orange, the VA continued to deny compensation improperly to over 31,000 veterans with just such claims. In fact, in promulgating the rules specified by Dioxin Standards Act, the VA not only confounded the intent of the Congress, but directly contradicted its own established practice of granting compensable service-connection status for diseases on the lesser showing of a statistical association, promulgating instead the more stringent requirement that compensation depends on establishing a cause and effect relationship.[31]

Mounting a challenge to the regulations, Veterans groups prosecuted a successful legal action which found that the VA had "both imposed an impermissibly demanding test for granting service connection for various diseases and refused to give the

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[31] See e.g. 38 C.F.R. § 3.310(b) (compensation granted for cardiovascular diseases incurred by veterans who suffered amputations of legs or feet); Nehmer at 1418.

The significance of the distinction between a statistical association and a cause and effect relationship is in the burden of proof that the veteran must satisfy in order to be granted benefits. A statistical association "means that the observed coincidence in variations between exposure to the toxic substance and the adverse health effects is unlikely to be a chance occurrence or happenstance," whereas the cause and effect relationship "describes a much stronger relationship between exposure to a particular toxic substance and the development of a particular disease than 'statistically significant association' does." Nehmer, 712 F.Supp. at 1416.

Thus, the regulation promulgated by the VA established an overly burdensome standard by incorporating the causal relationship test within the text of the regulation itself. 38 C.F.R. § 3.311(d) ("[s]ound scientific and medical evidence does not establish a cause and effect relationship between dioxin exposure" and any diseases except some cases of chloracne)(emphasis added).

veterans the benefit of the doubt in meeting the demanding standard." Nehmer v. U.S. Veterans Administration, 712 F. Supp. 1404, 1423 (1989) (emphasis in original). As a result, the court invalidated the VA's Dioxin regulation which denied service connection for all diseases other than chloracne; ordered the VA to amend its rules; and further ordered that the Advisory Committee reassess its recommendations in light of the court's order.[32]

Thus, on October 2, 1989, the VA amended 38 C.F.R. Part 1, which among other things set forth various factors for the Secretary and the Advisory Committee to consider in determining whether it is "at least as likely as not" that a scientific study shows a "significant statistical association" between a particular exposure to herbicides containing dioxin and a specific adverse health effect.[33] Equally important, the

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[32] Nehmer, 712 F. Supp at 1423.

[33] 38 C.F.R. § 1.17 (b) & (d). 38 C.F.R. § 1.17 states:
(a) From time to time, the Secretary shall publish evaluations of scientific or medical studies relating to the adverse health effects of exposure to a herbicide containing 2,3,7,8 tetrachlorodibenzo-p-dioxin (dioxin) and/or exposure to ionizing radiation in the "Notices" section of the Federal Register.
(b) Factors to be considered in evaluating scientific studies include:
(1) Whether the study's findings are statistically significant and replicable.
(2) Whether the study and its findings have withstood peer review.
(3) Whether the study methodology has been sufficiently described to permit replication of the study.
(4) Whether the study's findings are applicable to the veteran population of interest.
(5) The views of the appropriate panel of the Scientific Council of the Veteran' Advisory Committee on Environmental Hazards.
(c) When the Secretary determines, based on the evaluation of

regulation permits the Secretary to disregard the findings of the Advisory Committee, as well as the standards set forth at 38

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scientific or medical studies and after receiving the advice of the Veteran's Advisory Committee on Environmental Hazards and applying the reasonable doubt doctrine as set forth in paragraph (d)(1) of this section, that a significant statistical association exists between any disease and exposure to a herbicide containing dioxin or exposure to ionizing radiation, §§ 3.311a or 3.311b of this title, as appropriate, shall be amended to provide guidelines for the establishment of service connection.

(d)(1) For purposes of paragraph (c) of this section a "significant statistical association" shall be deemed to exist when the relative weights of valid positive and negative studies permit the conclusion that it is at least as likely as not that the purported relationship between a particular type of exposure and a specific adverse health effect exists.

(2) For purposes of this paragraph a valid study is one which:

(i) Had adequately described the study design and methods of data collection, verification and analysis;

(ii) Is reasonably free of biases, such as selection, observation and participation biases; however, if biases exist, the investigator has acknowledged them and so stated the study's conclusions that the biases do not intrude upon those conclusions; and

(iii) Has satisfactorily accounted for known confounding factors.

(3) For purposes of this paragraph a valid positive study is one which satisfies the criteria in paragraph (d)(2) of this section and whose findings are statistically significant at a probability level of .05 or less with proper accounting for multiple comparisons and subgroups analyses.

(4) For purposes of this paragraph a valid negative study is one which satisfies the criteria in paragraph (d)(2) of this section and has sufficient statistical power to detect an association between a particular type of exposure and a specific adverse health effect if such an association were to exist.

(e) For purposes of assessing the relative weights of valid positive and negative studies, other studies affecting epidemiological assessments including case series, correlational studies and studies with insufficient statistical power as well as key mechanistic and animal studies which are found to have particular relevance to an effect on human organ systems may also be considered.

(f) Notwithstanding the provisions of paragraph (d) of this section, a "significant statistical association" may be deemed to exist between a particular exposure and a specific disease if, in the Secretary's judgment, scientific and medical evidence on the whole supports such a decision.

C.F.R. § 1.17 (d) and determine in his own judgment that the scientific and medical evidence supports the existence of a "significant statistical association" between a particular exposure and a specific disease. 38 C.F.R. § 1.17 (f).

The Secretary recently exercised his discretionary authority under this rule when he found a significant statistical association between exposure to Agent Orange and non-Hodgkin's lymphoma, notwithstanding the failure of his own Advisory Committee to recommend such action in the face of overwhelming scientific data.[34]

B. THE WORK OF THE VETERANS' ADVISORY COMMITTEE ON ENVIRONMENTAL HAZARDS

To assess the validity and competency of the work of the Advisory Committee, I asked several impartial scientists to

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[34] After reviewing numerous scientific studies, at least four of which were deemed to be valid positive in demonstrating the link between exposure to herbicides containing dioxin and non-Hodgkin's lymphoma, the Advisory Committee still concluded that:

> The Committee does not find the evidence sufficient at the present time to conclude that there is a significant statistical association between exposure to phenoxy acid herbicides and non-Hodgkin's lymphoma. However, the Committee cannot rule out such an association.

The Secretary should be interested to note that a new mortality study positively confirms that farmers exposed to herbicides containing 2,4-D have an increased risk of developing non-Hodgkin's lymphoma. See Blair, "Herbicides and Non-Hodgkin's Lymphoma: New Evidence From a Study of Saskatchewan Farmers," 82 Journal of the National Cancer Institute 575-582 (1990).

review the Advisory Committee transcripts. Without exception, the experts who reviewed the work of the Advisory Committee disagreed with its findings and further questioned the validity of the Advisory Committee's review of studies on non-Hodgkin's lymphomas.

For instance, a distinguished group at the Fred Hutchinson Cancer Research Institute in Seattle, Washington, upon reviewing the Advisory Committee transcripts, concluded "that it is at least as likely as not that there is a significant association (as defined by the Secretary of Veterans Affairs) between [exposure to phenoxy acid herbicides and non-Hodgkin's lymphoma.]" [35] This same group further asserts that the Committee's work was "not sensible" and "rather unsatisfactory" in its review and classification of the various studies it reviewed. Additionally, these scientists regarded Dr. Lathrop's views as "less than objective" and felt that the possibility exists that "his extreme views (e.g., in respect to the role of dose-response testing) may have unduly affected the Committee's work." Finally, the Hutchinson scientists argue that the issue of chemical-specific effects, in which animal studies have been sufficient to demonstrate the carcinogenicity of dioxin, is an important factor "not well considered by the Committee." (emphasis in original)

A second reviewer of the Committee's work, Dr. Robert

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[35] Letter to Admiral Zumwalt from Dr. Robert W. Day, Director of the Fred Hutchinson Cancer Research Center of Seattle, Washington (Feb. 20, 1990).

Hartzman (considered one of the U.S. Navy's top medical researchers), effectively confirms the views of the Hutchinson group. Dr. Hartzman states that "the preponderance of evidence from the papers reviewed [by the Advisory Committee] weighs heavily in favor of an effect of Agent Orange on increased risk for non-Hodgkin's lymphoma."[36] Dr. Hartzman also attests that:

> an inadequate process is being used to evaluate scientific publications for use in public policy. The process uses scientific words like 'significant at the 5% level' and a committee of scientists to produce a decision about a series of publications. But in reality, the Committee was so tied by the process, that a decision which should have been based on scientific data was reduced to vague impressions... Actually, if the reading of the rules of valid negative found in the transcript is correct ('a valid negative must be significant at the p=.05 level' that is statistically significant on the negative side) none of the papers reviewed are valid negatives.[37]

A third reviewing team, Dr. Jeanne Mager Stellman, PhD (Physical Chemistry) and Steven D. Stellman, PhD (Physical Chemistry), also echo the sentiments expressed by the Hutchinson Group and Dr. Hartzman on the validity of the Committee's proceedings and conclusions. In fact, the Stellmans' detailed annotated bibliography and assessment of numerous cancer studies relevant to herbicide exposure presents a stunning indictment of the Advisory Committee's scientific interpretation and policy judgments regarding the link between Agent Orange and Vietnam

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[36] Letter to Admiral Zumwalt from Dr. R.J. Hartzman Capt. MC USN (March 7, 1990).

[37] Id. at p.3.

Veterans.[38]

A fourth reviewer, a distinguished scientist intimately associated with government sponsored studies on the effects of exposure to Agent Orange, states the same conclusions reached by the other reviewers:

> The work of the Veterans' Advisory Committee on Environmental Hazards, as documented in their November 2, 1989 transcript, has little or no scientific merit, and should not serve as a basis for compensation or regulatory decisions of any sort...
>
> My analysis of the NHL articles reviewed by the committee reveals striking patterns which indicate to me that it is much more likely than not that a statistical association exists between NHL and herbicide exposure.[39]

As these various reviewers suggest, the Advisory Committee's conclusions on the relationship between exposure to Agent Orange and non-Hodgkin's lymphoma were woefully understated in light of the clear evidence demonstrating a significant statistical association between NHL and exposure to phenoxy acid herbicides such as Agent Orange.

Perhaps more significant than the Committee's failure to make such obvious findings is the distressing conclusion of the independent reviewers that the Committee's process is so flawed

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[38] See Stellman & Stellman, "A Selection of Papers with Commentaries Relevant to the Science Interpretation and Policy: Agent Orange and Vietnam Veterans," (March 1, 1990). See also note 51 and accompanying text infra for additional discussion of the Stellmans' work.

[39] A copy of the anonymous reviewer's analysis can be made available for the Secretary's personal inspection and review. In another paper, this same source stated: "I estimate that the [Vietnam] Veterans are experiencing a 40% to 50% increase in sarcomas and non-Hodgkin's lymphoma rates."

as to be useless to the Secretary in making any determination on the effects of Agent Orange. From a mere reading of Committee transcripts, these reviewers detected overt bias in the Committee's evaluation of certain studies. In fact, some members of the Advisory Committee and other VA officials have, even before reviewing the evidence, publicly denied the existence of a correlation between exposure to dioxins and adverse health effects.[40] This blatant lack of impartiality lends credence to the suspicion that certain individuals may have been unduly influenced in their evaluation of various studies. Furthermore, such bias among Advisory Committee members suggests that the Secretary should, in accordance with the Dioxin Standards Act, appoint new personnel to the Advisory Committee.

III. THE CDC STUDIES

Were the faulty conclusions, flawed methodology and noticeable bias of the Advisory Committee an isolated problem, correcting the misdirection would be more manageable. But, experience with other governmental agencies responsible for specifically analyzing and studying the effects of exposure to

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[40] For instance, Dr. Lawrence B. Hobson (Director, Office of Environmental Medicine, Veterans Health Services and Research Administration), claims that TCDD "presents no threat from the exposures experienced by the veterans and the public at large," and virtually accuses scientists who find that such health effects do exist to be nothing more than witch doctors. See Hobson, "Dioxin and Witchcraft" presented at the 5th International Symposium on Chlorinated Dioxins and Related Compounds (September 1985).

Agent Orange strongly hints at a discernible pattern, if not outright governmental collaboration, to deny compensation to Vietnam Veterans for disabilities associated with exposure to dioxin.

A case in point is the Centers for Disease Control ("CDC"). As concerns grew following the first studies of human exposure to Agent Orange, Congress commissioned a large scale epidemiological study to determine the potential health effects for Vietnam Veterans exposed to Agent Orange. Initially, this study was to be conducted by the VA itself. When evidence surfaced, however, of the VA's footdragging in commencing the study (and initial disavowal of any potential harm from exposure to Agent Orange), Congress transferred the responsibility for the study to the CDC in 1983.[41]

Unfortunately, as hearings before the Human Resources and Intergovernmental Relations Subcommittee on July 11, 1989 revealed, the design, implementation and conclusions of the CDC study were so ill conceived as to suggest that political pressures once again interfered with the kind of professional, unbiased review Congress had sought to obtain.[42]

The Agent Orange validation study, for example, a study of

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[41] See 135 Congressional Record, Statement of Senator Tom Daschle (November 21, 1989); See also Agent Orange Hearings at p. 37.

[42] Oversight Review of CDC's Agent Orange Study: Hearing Before the Human Resources and Intergovernmental Relations Subcommittee of the Committee on Government Operations House of Representatives, 101st Cong., 1st Sess. at p. 71 and 330 (1989)[hereinafter cited as Agent Orange Hearing].

the long-term health effects of exposures to herbicides in Vietnam, was supposedly conducted to determine if exposure could, in fact, be estimated.[43] After four years and approximately $63 million in federal funds, the CDC concluded that an Agent Orange exposure study could not be done based on military records.[44] This conclusion was based on the results of blood tests of 646 Vietnam Veterans which ostensibly demonstrated that no association existed between serum dioxin levels and military-based estimates of the likelihood of exposure to Agent Orange.[45] Inexplicably, the CDC then used these "negative" findings to conclude that not only could an exposure study not even be done, but that the "study" which was never even conducted proves that Vietnam Veterans were never exposed to harmful doses of Agent Orange.

Even more disturbing, when the protocol for this "study" and the blood test procedures were examined further, there appeared to be a purposeful effort to sabotage any chance of a meaningful Agent Orange exposure analysis. For instance, the original protocol for the Agent Orange exposure study understandably called for subject veterans to be tracked by company level

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[43] Id. at 37; see also, Protocol for Epidemiologic Studies of the Health of Vietnam Veterans, Centers for Disease Control, Public Health Service, U.S. Department of Health and Human Services (November, 1983).

[44] Agent Orange Hearings at 13 (Statement of Dr. Vernon Houk).

[45] Id. at 12-13.

location.[46] By tracking company level units of 200 men, rather than battalions of 1,000 men, the location of men in relation to herbicide applications would be known with greater precision, thereby decreasing the probability that study-subjects would be misclassified as having been or not been exposed to Agent Orange.

However, in 1985 the CDC abruptly changed the protocol to have battalions, rather than companies, serve as the basis for cohort selection and unit location.[47] By the CDC's own admission, changing the protocol to track veterans on the broader battalion basis effectively diluted the study for the simple reason that many of the 1,000 men in a battalion were probably not exposed to Agent Orange. Why then did the CDC change the protocol in 1985?

According to Dr. Vernon Houk, Director of the Center for Environmental Health and Injury Control, the department within the CDC responsible for conducting the Agent Orange study, the protocol was changed because the CDC concluded that company-specific records were unreliable and contained too many gaps of information. As a result, military records could simply not be used to assess exposure.[48]

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[46] Id. at 41.

[47] Id. at 38.

[48] Agent Orange Hearing: Testimony of Dr. Vernon Houk at 38-40 and 69. Dr. Houk sports an unbounded skepticism for the health hazards of dioxin. He recently endorsed the lessening of the dioxin dumping standard in the State of Georgia at a rate 500 times more lenient than EPA recommended guidelines. See Letter from Dr. Vernon N. Houk to Leonard Ledbetter, Commissioner Georgia Department of Natural Resources (November 27, 1989).

Richard Christian, the former director of the Environmental Study Group of the Department of Defense ("ESG") testified that not only was this conclusion false, but that he had personally informed the CDC that adequate military records existed to identify company-specific movements as well as spray locations.[49] Furthermore, in a February 1985 report to the Congressional Office of Technology Assessment, the CDC reported that in analyzing 21 of 50 detailed computer HERBs tapes developed by the ESG on company movements that it was possible to correlate the exposure data to areas sprayed with Agent Orange with consistent results.[50] Indeed, a peer reviewed study sponsored by the American Legion conclusively demonstrated that such computerized data could be used to establish a reliable exposure classification system essential to any valid epidemiologic study of Vietnam Veterans.[51]

In addition to altering the protocol from company units to battalions, the CDC further diluted the study by changing the protocol on the length of time study subjects were to have served in Vietnam. Whereas the original protocol required subjects to have served a minimum of 9 months in combat companies, the CDC reduced the minimum to 6 months. Furthermore, the CDC eliminated

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[49] Agent Orange Hearing, Testimony of Richard Christian at 41.

[50] Interim Report, Agent Orange Study: Exposure Assessment: Procedures and Statistical Issues. See also American Legion Magazine Special Issue, "Agent Orange" (1990) at p. 12.

[51] Agent Orange Hearing 155-220 (Testimony of Steven and Jeanne Stellman); American Legion and Columbia University Vietnam Experience Study, Environmental Research (December, 1988).

from consideration all veterans who served more than one tour in Vietnam. Finally, while the original protocol called only for subjects who served in Vietnam from 1967 to 1968, the years that Agent Orange spraying was at its height, the CDC added an additional 6 months to this time period. The net effect of these various changes was seriously to dilute the possibility that study subjects would have been exposed to Agent Orange, which in turn would impair any epidemiological study's ability to detect increases in disease rate.[52]

Although the above referenced problems cast serious suspicion on the work of the CDC, perhaps its most controversial

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[52] Agent Orange Hearing at 46-49. This "dilution effect" is considered the classic flaw in epidemiological study design. Most epidemiologists would try to optimize the chances of observing an effect by including, rather than excluding, the subjects who are most likely to have been exposed to the suspected disease causing agent. This statistical ability to observe an effect if one is present is generally referred to as the "statistical power" of a given study.

When the CDC chose to generalize exposure to Agent Orange to groups of veterans who were less likely, rather than more likely, to be exposed, the power of the study was diluted. For example, if we assume that 1 out of every 5 men who served in Vietnam was exposed to Agent Orange, any possible effects of the exposure will be diluted when the 4 non-exposed men are averaged in. If we assume further that exposure to Agent Orange caused a doubling of the incidence of cancers among the 20% of men exposed, the effect would largely be obscured since 80% of the group being studied would not have been sprayed with Agent Orange and would thus have a normal background rate of cancer. Consequently, only exceptionally large increases in the cancer rate would be discovered and or reach statistical significance in a study group so diluted from the outset. See Agent Orange Hearing at 149 (Testimony of John F. Sommer, Jr., Director National Veterans Affairs and Rehabilitation Commission the American Legion).

See also Agent Orange Legislation and Oversight: Hearing Before the Committee on Veterans' Affairs, United States Senate, 100th Cong.,(May 12, 1988) (Testimony of Dr. Joel Michalek) at pp. 65, 66 and 668.

action was to determine unilaterally that blood tests taken more than 20 years after a veteran's service in Vietnam were the only valid means of determining a veteran's exposure to Agent Orange. In addition, Dr. Houk further "assumed" that the half-life for dioxin in the blood was seven years.[53] When the underlying data for Houk's assumptions were recently reviewed, however, 11 percent of the blood tests were invalid (i.e. study subjects had higher values of dioxin in their blood in 1987 than in 1982 even though the subjects had no known subsequent exposure to dioxin) and the half lives of dioxin in the remaining study subjects ranged from a low of 2 to a high of 740 years![54] Yet despite this tremendous variance in the data and the high incidence of false results, Houk and the CDC concluded, rather remarkably, that a large scale exposure study was simply not possible since "negative" blood tests appeared to "confirm" that study subjects were not even exposed to Agent Orange.

Such conclusions are especially suspect given the fact that scientists have consistently cautioned against the use of blood tests as the sole basis for exposure classification. Although blood and adipose tissue tests can be used to confirm that

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[53] Agent Orange Hearing at 59. Dr. Houk's assumption was based on a study of only 36 former Ranch Handers (members of "Operation Ranch Hand," the Air Force herbicide defoliation program) who had volunteered blood samples in 1982 and 1987.

[54] American Legion Magazine Reprint "Agent Orange" at 12 See also, Agent Orange Hearing at p. 67 (testimony of Dr. Houk revealed that the senior statistician on the Agent Orange project believed that the dioxin blood analysis was so flawed there is a substantial likelihood that there is no correlation between the exposure scores and the blood levels).

Vietnam Veterans were heavily exposed to Agent Orange and the contaminant dioxin[55], even the CDC's own researchers have unequivocally stated that "much more has to be learned about the kinetics of dioxin metabolism and half-life before current levels can be used to fully explain historic levels of exposure."[56]

While the CDC's changes in protocol have been "justified", however unreasonably, on the basis of "scientific" explanations[57], what cannot be justified is the evidence of political interference in the design, implementation and drafting of results of the CDC study by Administration officials rather than CDC scientists. As early as 1986, the Subcommittee on Oversight and Investigations of the Committee on Energy and Commerce documented how untutored officials of the Office of Management and Budget (OMB) interfered with and second-guessed the professional judgments of agency scientists and multidisciplinary panels of outside peer review experts

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[55] See Kahn, "Dioxins and Dibenzofurans in Blood and Adipose Tissue of Agent Orange Exposed Vietnam Veterans and Matched Controls," 259 Journal of the American Medical Association 1661 (1988). This report found that "Vietnam veterans who were heavily exposed to Agent Orange exceeded matched control subjects in both blood and adipose tissue levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) but not in the levels of the 12 other 2,3,7,8-substituted dioxins and dibenzofurans that were detected. Since only TCDD among these compounds was present in Agent Orange but all are present in the population of the industrialized world, it is likely that the elevated TCDD levels arose from wartime exposure."

[56] Patterson, "Levels of Polychlorinated Dibenzo-p-dioxins and Dibenzofurans in Workers Exposed to 2,3,7,8 - tetrachlorodibenzo-p-dioxin, 16 American Journal of Industrial Medicine 135, 144 (1989).

[57] See generally, Agent Orange Hearing (Testimony of Dr. Vernon Houk) at 44-50.

effectively to alter or forestall CDC research on the effects of Agent Orange, primarily on the grounds that "enough" dioxin research had already been done.[58] These Agent Orange Hearings revealed additional examples of political interference in the CDC's Agent Orange projects by members of the White House Agent Orange Working Group.[59]

Dr. Philip J. Landrigan, the former Director of the Environmental Hazards branch at the CDC, upon discovering the various irregularities in CDC procedures concluded that the errors were so egregious as to warrant an independent investigation not only of the methodology employed by the CDC in its validation study, but also a specific inquiry into what actually transpired at the Center for Environmental Health of the CDC.[60]

With these suspicions in mind, it should come as no surprise that those familiar with the CDC's work found little credence in the conclusions reached by the CDC in its recently released Selected Cancers Study. Even though the CDC has previously stated that it believes exposure to Agent Orange is impossible to assess, it found no difficultly in reporting to the press upon the release of the Selected Cancers Study that exposure to Agent

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[58] OMB Review of CDC Research: Impact of the Paperwork Reduction Act; A Report Prepared for the Subcommittee on Oversight and Investigations of the Committee on Energy and Commerce, 99th Cong. 2nd Sess. (October 1986).

[59] See Agent Orange Hearing at 49-54 (Testimony of Dr. Vernon Houk).

[60] Agent Orange Hearing at 229 and 330.

Orange does not cause cancer. This conclusion was reached despite the fact that the CDC made no effort to determine, through military records or blood/adipose tissue tests, if study subjects were, indeed, exposed to dioxins; nor did the CDC attempt to verify exposure to Agent Orange of those study subjects who actually contracted cancerous diseases. In fact, according to scientists who have made preliminary reviews of the CDC's findings, the statistical power of any one cancer grouping, with the exception of non-Hodgkin's lymphoma, was so low as to make any conclusion virtually impossible.

IV. RANCH HAND STUDY

Unfortunately, political interference in government sponsored studies associated with Agent Orange has been the norm, not the exception. In fact, there appears to have been a systematic effort to suppress critical data or alter results to meet preconceived notions of what alleged scientific studies were meant to find.[61] As recently as March 9, 1990 Senator Daschle disclosed compelling evidence of additional political interference in the Air Force Ranch Hand study, a separate government sponsored study meant to examine the correlation between exposure to Agent Orange and harmful health effects among Air Force veterans who participated in Agent Orange spraying

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[61] See generally Agent Orange Hearing; Congressional Record, S 2550 (March 9, 1990); Congressional Record, (November 21, 1989) (Statements of Senator Thomas Daschle).

missions under Operation Ranch Hand. As Senator Daschle explained:

> In January 1984, the scientists in charge of the Ranch Hand Study issued a draft baseline morbidity report that described some very serious health problems in the Ranch Hand veterans and stated that the Ranch Handers, by a ratio of five to one, were generally less well than the veterans in the control group. The opening sentence of the draft report's conclusion was clearly stated: "It is incorrect to interpret this baseline study as 'negative.' "
>
> After the Ranch Hand Advisory Committee, which operates under the White House Agent Orange Working Group of the Domestic Policy Council, got its hands on the document, the final report was changed in some very important ways. Most notably, the table and exposition explaining that the Ranch Handers were generally less well than the controls was omitted, and the final conclusion was altered substantially. The statement that the baseline study was not negative was completely omitted and the study was described as "reassuring." [62]

By altering the study's conclusion, opponents of Agent Orange compensation were able to point to "irrefutable proof" that Agent Orange is not a health problem: if those veterans most heavily exposed to Agent Orange did not manifest any serious health problems, they argued, then it could safely be deduced that no veteran allegedly exposed to Agent Orange in smaller doses could have health problems. Yet, when Senator Daschle questioned Air Force scientists on why discrepancies existed between an Air Force draft of the Ranch Hand Study and the final report actually released to the press, the answers suggested not merely disagreements in data evaluation, but the perpetration of fraudulent conclusions. In a word, the major premise was badly

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[62] See Congressional Record S 2550 (March 9, 1990).

flawed.

For example, in 1987 Ranch Hand scientists confirmed to Senator Daschle that an unpublished birth defects report shows that birth defects among Ranch Hand children are double those of children in the control group and not "minor" as originally reported in 1984.[63]

This increase in birth defects takes on added significance when one considers that the original CDC birth defects study, which found no increase in birth defects, merely examined birth defects as reported on birth certificates, rather than as reported by the child's parent or physician. The CDC never recorded hidden birth defects, such as internal organ malformations and other disabilities that only became apparent as the child developed. Consequently, it is very likely that the CDC's negative findings on birth defects were also vastly understated.[64]

In addition to elevated birth defects, Ranch Handers also showed a significant increase in skin cancers unrelated to overexposure to the sun as originally suggested in the 1984 report. Air Force scientists also admitted that Air Force and White House Management representatives were involved in

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[63] Congressional Record, (November 21, 1989) (Statement of Senator Thomas Daschle).

[64] The CDC birth defects study was confined to Vietnam Veterans located in the Atlanta, Georgia region. The study was not an Agent Orange birth defects study since no effort was made to determine whether the veterans had even been exposed to Agent Orange. See notes 10 and 18 supra for additional information on birth defects.

scientific decisions in spite of the study's protocol which prohibited such involvement.[65]

On February 23, 1990, the Air Force released a follow-up morbidity report on the Ranch Handers. That report, "1987 Followup Examination Results," described statistically significant increases in health problems among Ranch Handers including: all cancers -- skin and systemic combined, both verified and suspected; skin cancers alone; hereditary and degenerative neurological diseases and other problems. The Air Force concluded, however, that these and other problems cannot necessarily be related to Agent Orange/dioxin exposure, as they do not always show a "dose-response" relationship - particularly since the exposure index used in the data analysis "is not a good measure of actual dioxin exposure." [66]

With this conclusion, the Air Force for the first time officially acknowledged that the conclusions reached in its original 1984 Ranch Hand study are not simply moot, but that the Ranch Hand study is not, at this date, an Agent Orange study at all since dioxin exposure could not be determined reliably in the first place. In other words, the Air Force could just as easily have concluded that the health problems associated with the Ranch Handers were not necessarily related to eating beer nuts.

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[65] Congressional Record, S 2551 (March 9, 1990) (Statement of Senator Daschle).

[66] Wolfe, et. al., Air Force Health Study and Epidemiologic Investigation of Health Effects in Air Force Personnel Following Exposure to Herbicides (Feb. 1990) at p. vi.

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For the Air Force to have made the statement in 1990 of no evidence of a link between exposure to Agent Orange and the cancer problems experienced by Ranch Handers is, as Senator Daschle notes, "patently false."[67]. Although not yet conclusive, what the Ranch Hand and CDC studies demonstrate is that there is evidence of a link between health problems and dioxin exposures which may become definitive when a new and reliable exposure index is used to evaluate the data.

As stated by Dr. James Clary, one of the scientists who prepared the final Ranch Hand report:

> The current literature on dioxin and non-Hodgkin's lymphoma and soft tissue sarcoma can be characterized by the following:
>
> 1. It underestimates (reduced risk estimates) the effect of dioxins on human tissue systems. As additional studies are completed we can expect to see even stronger correlations of dioxin exposure and NHL/STS.
>
> 2. Previous studies were not sensitive enough to detect small, but statistically significant increases in NHL/STS. As time progresses, and additional evidence is forthcoming, it will be increasingly difficult for anyone to deny the relationship between dioxin exposure and NHL/STS.[68]

V. INDEPENDENT STUDIES

Shamefully, the deception, fraud and political interference that has characterized government sponsored studies on the health

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[67] Congressional Record S. 2551 (March 9, 1990). See also Letter from Maj. Gen James G. Sanders, U.S.A.F. Deputy Surgeon General to Senator Thomas Daschle (February 23, 1990).

[68] Letter from Dr. James Clary to Senator Tom Daschle (September 9, 1988).

effects of exposure to Agent Orange and/or dioxin has not escaped studies ostensibly conducted by independent reviewers, a factor that has only further compounded the erroneous conclusions reached by the government.

For instance, recent litigation against the Monsanto corporation revealed conclusive evidence that studies conducted by Monsanto employees to examine the health effects of exposure to dioxin were fraudulent. These same fraudulent studies have been repeatedly cited by government officials to deny the existence of a relationship between health problems and exposure to Agent Orange. According to court papers:

> Zack and Gaffey, two Monsanto employees, published a mortality study purporting to compare the cancer death rate amongst the Nitro workers who were exposed to Dioxin in the 1949 explosion with the cancer death rate of unexposed workers. The published study concluded that the death rate of the exposed worker was exactly the same as the death rate as the unexposed worker. However, Zack and Gaffey deliberately and knowingly omitted 5 deaths from the exposed group and took 4 workers who had been exposed and put these workers in the unexposed group, serving, of course, to decrease the death rate in the exposed group and increase the death rate in the unexposed group. The exposed group, in fact, had 18 cancer deaths instead of the reported 9 deaths (Pl. Ex. 1464), with the result that the death rate in the exposed group was 65% higher than expected (emphasis in original).[69]

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[69] Brief of Plaintiffs-appellees in Kemner, et. al. v. Monsanto Company, No. 5-88-0420 (5th Dist., Illinois Appellate Court) (Oct. 3, 1989) (as the facts were proven at trial, the appeal only considered appealable matters of law). Plaintiff's brief refers to Zack and Gaffey, "A Mortality Study of Workers Employed at the Monsanto Company Plant in Nitro, WV," Human and Environmental Risks of Chlorinated Dioxins and Related Compounds (1983) pp. 575-591. It should be noted that the Advisory Committee classified this report as "negative" in evaluating compensation for NHL.

The brief also states that another study of the workers exposed in the 1949 accident was also fraudulent (e.g. R.R. Suskind

Similarly, recent evidence also suggests that another study heavily relied upon by those opposed to Agent Orange compensation to deny the existence of a link between dioxin and health effects was falsified. Three epidemiologic studies and several case report studies about an 1953 industrial accident in which workers at a BASF plant were exposed to dioxins concluded that exposure to TCDD did not cause human malignancies.[70] A reanalysis of the data that comprised the studies, all of which was supplied by the BASF company itself, revealed that some workers suffering from chloracne (an acknowledged evidence of exposure to dioxin) had actually been placed in the low-exposed or non-exposed cohort groups. Additionally, 20 plant supervisory personnel, not believed to have been exposed, were placed in the exposed group.

When the 20 supervisory personnel were removed from the exposed group, thereby negating any dilution effect, the reanalysis revealed statistically significant increases in cancers of the respiratory organs (lungs, trachea, etc.) and

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and V.S. Hertzberg, "Human Health Effects of 2,4,5-T and Its Toxic Contaminants," Journal of the American Medical Association, Vol. 251, No. 18 (1984) pgs. 2372-2380.) The study reported only 14 cancers in the exposed group and 6 cancers in the unexposed group. Trial records conclusively demonstrated, however, that there were 28 cancers in the group that had been exposed to dioxins, as opposed to only 2 cancers in the unexposed group.

[70] See, e.g. Thiess, Frentzel-Beyme, Link, "Mortality Study of Persons Exposed to Dioxin in a Trichlorophenol Process Accident that Occurred in the BASF AG on November 17 , 1953", 3 American Journal of Industrial Medicine 179-189 (1982)

cancers of the digestive tract.[71] According to the scientist who conducted this study, "[t]his analysis adds further evidence to an association between dioxin exposure and human malignancy."[72]

Recent evidence also reveals that Dow Chemical, a manufacturer of Agent Orange was aware as early as 1964 that TCDD was a byproduct of the manufacturing process. According to Dow's then medical director, Dr. Benjamin Holder, extreme exposure to dioxins could result in "general organ toxicity" as well as "psychopathological" and "other systemic" problems.[73] In fact, a

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[71] Friedemann Rohleder, "Dioxins and Cancer Mortality Reanalysis of the BASF Cohort," presented at the 9th International Symposium on Chlorinated Dioxins and Related Compounds, Toronto, Ontario (Sept. 17-22, 1989). BASF recently published a study in an attempt to refute the allegations that the original studies related to the accident were fraudulent. See Zobier, Messerer & Huber, "Thirty Four Year Mortality Follow Up of BASF Employees, 62 Occupational Environmental Health 139-157, (Oct. 19, 1989). While the company states that "there was no significant increase in deaths from malignant neoplasms," the study does conclude that:

> There was, however, a significant excess for all cancers combined among the chloracne victims 20 or more years after initial exposure when an excess would be most likely to occur. In addition, there is the notable finding on one case of liver cancer without cirrhosis in a worker with an exceptionally high level of TCDD in the blood.

Id. at 155. See also id. at 139 ("In general, our results do not appear to support a strong association between cancer mortality and TCDD, but they do suggest that some hazard may have been produced.") (emphasis added) and 149 ("Although TCDD blood levels were available for only 5 of the 10 subjects, the three highest levels were found in subjects with liver cancer, leucosis and Merkell-cell carcinoma of the skin.").

[72] Wanchinski, "New Analysis Links Dioxin to Cancer," New Scientist, (Oct. 28, 1989) p. 24.

[73] See L. Casten, Patterns of Secrecy: Dioxin and Agent Orange (1990) (unpublished manuscript detailing the efforts of government and industry to obscure the serious health consequences of exposure to dioxin).

recent expert witness who reviewed Dow Chemical corporate documents on behalf of a plaintiff injured by exposure to dioxin who successfully sued Dow[74] states unequivocally that "the manufacturers of the chlorphenoxy herbicides have known for many years about the adverse effects of these materials on humans who were exposed to them."[75]

VI. CURRENT SCIENCE ON HEALTH EFFECTS OF HERBICIDES AND DIOXIN

Despite its poor record in carrying out its responsibility to ascertain the health effects of exposure to Agent Orange, the CDC has been candid in some of its findings. As early as 1983, for instance, the CDC stated in the protocol of its proposed Agent Orange Studies "[t]hat the herbicide contaminant TCDD is considered to be one of the most toxic components known. Thus any interpretation of abnormal findings related to 2,4,5-T must take into consideration the presence of varying or undetermined

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[74] Peteet v. Dow Chemical Co., 868 F.2d 1428 (5th Cir. 1989) cert denied 110 S.Ct. 328 (1989).

[75] Letter from Daniel Teitelbaum, M.D., P.C. to Admiral E.R. Zumwalt, Jr. (April 18, 1990). Dr Teitelbaum additionally states:

> What I do think...may bear on the Agent Orange issue, is the fact that in review of Dow's 2,4-D documentation I found that there are significant concentrations of potentially carcinogenic materials present in 2,4-D which have never been made known to the EPA, FDA, or to any other agency. Thus, in addition to the problem of the TCDD which, more likely than not, was present in the 2,4,5-T component of Agent Orange, the finding of other dioxins and closely related furans and xanthones in the 2,4-D formulation was of compelling interest to me.

amounts of TCDD." [76]

In 1987, after first being leaked by the New York Times, a VA mortality study was released indicating a 110 percent higher rate of non-Hodgkin's lymphoma in Marines who served in heavily sprayed areas as compared with those who served in areas that were not sprayed.[77] The study also found a 58 percent higher rate of lung cancer among the same comparative groups.[78]

Also in 1987, a second VA study found a suggestive eight-fold increase in soft tissue sarcoma among veterans most likely to

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[76] CDC Protocol, see note 1 supra. The CDC went on to state that a wide variety of health effects have been observed following the administration of TCDD to experimental animals including soft tissue sarcomas and lymphoma, nasal and nasopharyngeal cancers, birth defects, changes in thymus and lymphoid tissues, and other numerous cancers. Additionally, the CDC acknowledged the toxic effects of occupational exposure to dioxin, including evidence that exposure "may be associated with an increased risk of soft tissue sarcoma and lymphoma" and perhaps nasal and nasopharyngeal cancers.

[77] Breslin, et. al. "Proportionate Mortality Study of U.S. Army and U.S. Marine Corps Veterans of the Vietnam War," Veterans Administration (1987).

[78] Id. Some scientists, including the Advisory Committee have attempted to denigrate these significant findings on the basis that Army personnel did not show similar results. The explanation for this lack of comparative Army findings is directly attributable to the dilution effect caused by including logistics personnel as part of the Army study. Marines were studied as a separate group. The Marine's logistical support personnel (i.e. the Navy), were not included. Thus, the increased cancers among Marines were clearly associated with field exposure to Agent Orange.

The Army study, on the other hand, combined field personnel with personnel on logistics assignments who were unlikely to have been exposed to Agent Orange. As a result, the Army findings were drastically diluted. Additionally, Army personnel generally engaged the enemy and returned to base, whereas Marines consistently remained in areas presumably sprayed by Agent Orange to provide medical, health and engineering assistance to the local population. Such "pacification" efforts gave Marines additional opportunities to be exposed to dioxins.

have been exposed to Agent Orange.[79]

A proportionate mortality study of deaths in pulp and paper mill workers in New Hampshire from 1975 to 1985 showed that one or more of the exposures experienced by such workers (dioxin is a byproduct of pulp and paper production) posed a "significant risk" for cancers of the digestive tract and lymphopoietic tissues.[80]

Another case control study of farmers in Hancock County, Ohio, showed a "statistically significant" rise in Hodgkin's disease and non-Hodgkin's lymphoma. Although the study speculates that exposure to phenoxy herbicides may be the cause of such elevated cancers, the study recognizes that, given the size of its cohort, the only credible conclusion that can be drawn is that it "adds to the growing body of reports linking farming and malignant lymphoma, particularly NHL." [81]

A study of disease and non-battle injuries among U.S. Marines in Vietnam from 1965 to 1972 showed a significantly higher rate of first hospitalizations for Marines stationed in Vietnam as opposed to Marines stationed elsewhere, particularly

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[79] Kang, et. al., "Soft-Tissue Sarcoma and Military Service in Vietnam: A Case Control Study," 79 Journal of the National Cancer Institute 693 (October, 1987). The increases were not statistically significant as reported. Nonetheless, the results are remarkable.

[80] E. Schwartz, "A Proportional Mortality Ratio of Pulp and Paper Mill Workers in New Hampshire," 45 British Journal of Industrial Medicine, 234-238 (1988).

[81] Dubrow, Paulson & Indian, "Farming and Malignant Lymphoma in Hancock County, Ohio," 45 British Journal of Industrial Medicine, 25-28 (1988).

for neoplasms, diseases of the blood and blood forming organs and diseases of the circulatory and respiratory systems.[82] Of particular significance is the fact that the rate of first hospitalization for disease and non-battle injuries among Vietnam personnel rose steadily, reaching a peak in 1969, while the rate of non-Vietnam personnel remained relatively constant.[83] This rise in hospitalization for non-combat injuries coincides exactly with the increased use of Agent Orange, reaching a peak in 1969, and declining thereafter until its elimination in 1971.

In a recently published article entitled "2,4-D, 2,4,5 -T, and 2,3,7,8 -TCDD: An Overview", the authors acknowledge that at least three weaknesses in research related to dioxins are sufficient to cast doubt on the validity of any study.[84] The

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[82] Palinkas & Coben, "Disease and Non-Battle Injuries Among U.S. Marines in Vietnam, 153 Military Medicine 150 (March, 1988).

[83] Id. at 151. It should be noted that the year of greatest combat activity, as measured by the number of personnel wounded in action, 1968, had the smallest disease and non-battle injury vs. wounded in action ratio. Id. at 152.

[84] Lilienfeld and Gallo "2,4-D, 2,4,5-T and 2,3,7,8-TCDD: An Overview," Epidemiologic Review, Vol. II (1989). Three major criteria must be considered in evaluating the numerous epidemiologic studies of phenoxy herbicides and 2,3,7,8-TCDD: 1) the accuracy of exposure assessment; 2) the studies' statistical power; and 3) the adequacy of follow-up. Problems in any one of the three areas leaves the study open to criticism and subject to manipulation.

For instance, in retrospective studies, various proxies of exposure to herbicides and 2,3,7,8,-TCDD have been used such as military service in Vietnam or residence in an area in which the herbicides were sprayed. The weakness in such an approach is that unless the proxy corresponds to exposure, the "exposed group" is diluted with the individuals who have NOT been exposed, thereby reducing the magnitude of the strength of the association. In fact, such reduction may be of such a degree as to preclude detection of any effect. The authors note, however, that the recent development

authors report that while the data on soft tissue sarcoma and phenoxy acids are too inconsistent to allow for any comment at this time, there is evidence of a strong association between STS and the suspect chemicals in 2 of the 8 studies analyzed in their article. Furthermore, the birth defect studies analyzed "suggest that adverse reproductive effects can be caused by [dioxin]."[85]

Recent studies in Vietnam continue to show statistically significant reproductive anomalies and birth defects among women, and children of women presumably exposed to Agent Orange spraying.[86]

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of a serum marker for 2,3,7,8-TCDD by Kahn may provide the means of identifying persons who have been exposed.

Furthermore, studies concerning Agent Orange have nearly all been conducted in the past decade. This 10 year latency period is generally thought to be insufficient for many cancers to be clinically detected.

[85] Id.

[86] See note 10 supra. It should be noted that as early as 1977 information about Agent Orange's potential for genetic damage was known to the VA. For example, a "NOT FOR RELEASE" VA document expressly noted Agent Orange's "high toxicity" and "its effect on newborn, deformed children -- similar to the thalidomide situation." See L. Casten, Patterns of Secrecy note 73 supra at Department of Veteran Affairs p.4. Similarly, in March of 1980, Senator Tom Daschle and Rep. David Bonior received an anonymous memorandum written on VA stationery which stated:

> chemical agents 2,4,5-T and 2,4-D commonly known as Agent Orange and Agent Blue, are mutagenic and teratogenic. This means they intercept the genetic DNA message processed to an unborn fetus, thereby resulting in deformed children being born. Therefore, the veteran would appear to have no ill effects from the exposure but he would produce deformed children due to this breakage in his genetic chain....Agent Orange is 150,000 times more toxic than organic arsenic.

Id. See also Wolfe & Lathrop, "A Medical Surveillance Program for Scientists Exposed to Dioxins and Furans," Human and Environmental Risks of Chlorinated Dioxins and Related Compounds, 707-716 (1983)

In the December 1, 1989, issue of Cancer, a study of the cancer risks among Missouri farmers found elevated levels of lip and bone cancer as well as nasal cavity and sinuses, prostrate, non-Hodgkin's lymphoma and multiple myeloma. Smaller elevations, but elevations nonetheless, were found for cancers of the rectum, liver, malignant melanoma, kidney and leukemia. According to the authors, evidence of the cause for the elevated risks for these illnesses "may be strongest for a role of agricultural chemicals, including herbicides, insecticides and fertilizers." [87]

Both the U.S. Environmental Protection Agency (EPA) and the International Agency for Research on Cancer (IARC) have concluded that dioxin is a "probable human carcinogen." [88]

In a work entitled "Carcinogenic Effects of Pesticides" to be issued by the National Cancer Institute Division of Cancer Etiology, researchers conclude that while confirmatory data is lacking there is ample evidence to suggest that NHL, STS, colon, nasal and nasopharyngeal cancer can result from exposure to phenoxy herbicides.

A just released case control study of the health risks of exposure to dioxins confirmed previous findings that exposure to

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(Proceedings of International Symposium on Chlorinated Dioxins and Related Compounds, Arlington, VA, October 25-29, (1981)). The article explains the possible mechanism for paternally transmitted birth defects.

[87] Brownson, et. al. "Cancer Risks Among Missouri Farmers," 64 Cancer 2381, 2383 (December 1, 1989).

[88] Agency for Toxic Substances and Disease Registry, pp. 7,, 61-68, 94 reprinted in Rachel's Hazardous Waste News # 173 (March 21, 1990)

phenoxyacetic acids or chlorophenols entails a statistically significant increased risk (i.e. 1.80) for soft tissue sarcoma.[89]

As recently as February 28, 1990 an additional study found that farmers exposed to various herbicides containing 2,4-D may experience elevated risks for certain cancers, particularly cancers of the stomach, connective tissue, skin, brain, prostate, and lymphatic and hematopoietic systems."[90]

This week a scientific task force, after reviewing the scientific literature related to the potential human health effects associated with exposure to phenoxyacetic acid herbicides and/or their associated contaminants (chlorinated dioxins) concluded that it is at least as likely as not that exposure to Agent Orange is linked to the following diseases: non-Hodgkin's lymphoma, soft tissue sarcoma, skin disorders/chloracne, subclinical hepatotoxic effects (including secondary coproporphyrinuria and chronic hepatic porphyria), porphyria cutanea tarda, reproductive and developmental effects, neurologic

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[89] Eriksson, Hardell & Adami, "Exposure to Dioxins as a Risk Factor for Soft Tissue Sarcoma: A Population-Based Case-Control Study," 82 Journal of the National Cancer Institute 486-490 (March 21, 1990). It should be noted that in this study the median latency for phenoxyacetic acid and chlorophenols exposure was 29 and 31 years respectively, thereby suggesting that many of the veterans who are at risk have not yet manifested symptoms of STS.

[90] Blair, "Herbicides and Non-Hodgkin's Lymphoma: New Evidence From a Study of Saskatchewan Farmers," 82 Journal of the National Cancer Institute 575-582 (1990).

effects and Hodgkin's disease.[91]

On the same day that this scientific task force reported a statistically significant linkage between exposure to the dioxins in Agent Orange and various cancers and other illnesses, the Environmental Protection Agency reported that the cancer risk posed by the release of such a "potent carcinogen" as dioxin in the production of white paper products is "high enough to require tighter controls on paper mills."[92]

CONCLUSIONS

As many of the studies associated with Agent Orange and dioxins attest, science is only at the threshold of understanding the full dimension of harmful toxic effects from environmental agents on various components of the human immune system.[93] In

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[91] Report of the Agent Orange Scientific Task Force of the American Legion, Vietnam Veterans of America, and the National Veterans Legal Services Project, reported by McAllister, "Viet Defoliant Linked to More Diseases, Washington Post, May 1, 1990 at A8, col. 4. The report also found that there are other disorders for which there is evidence suggesting an association with exposure to Agent Orange, but for which statistically significant evidence is not currently available. Those diseases include: leukemias, cancers of the kidney, testis, pancreas, stomach, prostate, colon hepatobiliary tract, and brain, psychosocial effects, immunological abnormalities, and gastrointestinal disorders.

[92] Weisskopf, "EPA Seeking to Reduce Dioxin in White Paper: Cancer Risk Said to Justify Mill Restrictions," Washington Post, May 1, 1990 at A8, col. 1.

[93] A recent report in the Washington Post suggests that there is an inherent uncertainty in trying to measure the dangers posed by the chemicals humans eat, drink and breathe. Since human experimentation is impossible to assess the effect of varied doses of a chemical on human health, scientists are ultimately required

fact, a whole new discipline - immunotoxicology - has developed to explore further the effects of environmental chemicals on human health and to relate animal test results to humans.[94]

Immunotoxicology has established, however, at a minimum that at least three classes of undesirable effects are likely occur when the immune system is disturbed by environmental exposure to chemicals such as dioxin, including: 1) immunodeficiency or suppression; 2) alteration of the host defense mechanism against mutagens and carcinogens (one theory is that the immune system detects cells altered by mutagens or other carcinogenic trigger and destroys these cells. Thus, an impaired immune system may not detect and destroy a newly forming cancer); and 3) hypersensitivity or allergy to the chemical antagonist. Because of dioxin's ability to be both an immunosuppressant and a carcinogen, as early as 1978 immunologists were suggesting that "[a]gents such as TCDD...may be far more dangerous than those possessing only one of these properties."[95]

While scientists are not in agreement, some immunotoxicologists argue that one molecule of a carcinogenic agent, like dioxin in the right place and at the right time can

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to speculate or guess as to the health effects of a given chemical to the human body. See Measuring Chemicals' Dangers: Too Much Guesswork?" Washington Post, March 23, 1990.

[94] Silbergeld & Gaisewicz, "Dioxins and the Ah Receptor," 16 American Journal of Industrial Medicine 455, 468-69 (1989).

[95] Inadvertent Modification of the Immune Response - The Effect of Foods, Drugs, and Environmental Contaminants; Proceedings at the Fourth FDA Symposium; U.S. Naval Academy (August 28-30, 1978), p. 78.

cause the human immune system to turn on itself, manifesting such breakdowns in the form of cancer. Indeed, even some courts have accepted this theory of causation in matters specifically related to exposure to dioxin.[96]

With additional evidence from Vietnam suggesting that Agent Orange contaminants have the ability to migrate away from actual spray locations via river channels and the food chain, the opportunity for a Vietnam Veteran to have been exposed to dioxin contaminant molecules increases significantly.[97]

It cannot be seriously disputed that any large population exposed to chemical agents, such as Vietnam Veterans exposed to Agent Orange, is likely to find among its members a number who will develop malignancies and other mutagenic effects as a result of being exposed to harmful agents.

To be sure, decisions today with regard to the seriousness of Agent Orange health effects must be made while the science of

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[96] See Peteet v. Dow Chemical Co., 868 F.2d 1428, 1433 (5th Cir. 1989) cert denied 110 S.Ct. 328 (1989).

[97] See e.g. Schecter, et. al., "Levels of 2,3,7,8-TCDD in Silt Samples Collected Between 1985-86 From Rivers in the North and South of Vietnam," 19 Chemosphere, 547-550 (1989) (suggestive findings that the predominant dioxin isomer in Agent Orange has moved into downstream rivers in the South of Vietnam); Olie, et. al., "Chlorinated Dioxin and Dibenzofuran Levels in Food and Wildlife Samples in the North and South of Vietnam," 19 Chemosphere 493-496 (1989) (food and wildlife specimens in South Vietnam had a higher relative abundance of 2,3,7,8-TCDD suggesting contamination from Agent Orange); Schecter, et. al. "Chlorinated Dioxin and Dibenzofuran Levels in Food Samples Collected Between 1985-87 in the North and South of Vietnam," 18 Chemosphere 627-634 (1989) (Agent Orange contaminants, specifically 2,3,7,8-TCDD found at relatively elevated levels in food and wildlife samples 15-25 years after environmental contamination with compound in South of Vietnam).

immunotoxicology is in its infancy. After having evaluated and considered all of the known evidence on Agent Orange and dioxin contaminants, it is evident to me that enough is known about the current trends in the study of dioxins, and their linkage with certain cancers upon exposure, to give the exposed Vietnam Veteran the benefit of the doubt.

This benefit of the doubt takes on added credence given two separate means for determining exposure to Agent Orange - 1) HERBs and Service HERBs tapes establishing troop location for comparison with recorded Ranch Hand spraying missions; and 2) blood testing from living veterans to ascertain elevated dioxin levels. The inexplicable unwillingness of the CDC to utilize this data has had the effect of masking the real increase in the rate of cancers among the truly exposed. There is, in my opinion, no doubt that had either of these methods been used, statistically significant increased rates of cancer would have been detected among the Veterans for whom exposure can still be verified.

Since science is now able to conclude with as great a likelihood as not that dioxins are carcinogenic directly and indirectly through immunosuppression, and since a large proportion of those exposed to dioxin can be so ascertained, I am of the view that the compensation issue for service-related illnesses associated with exposure to Agent Orange should be resolved in favor of Vietnam Veterans in one of the two following ways:

COMPENSATION FOR SERVICE RELATED ILLNESSES

Alternative 1:

Any Vietnam Veteran, or Vietnam Veteran's child who has a birth defect, should be presumed to have a service-connected health effect if that person suffers from the type of health effects consistent with dioxin exposure and the veteran's health or service record establishes 1) abnormally high TCDD in blood tests; or 2) the veteran's presence within 20 kilometers and 30 days of a known sprayed area (as shown by HERBs tapes and corresponding company records); or 3) the veteran's presence at fire base perimeters or brown water operations where there is reason to believe Agent Orange have occurred.

Under this alternative compensation would not be provided for those veterans whose exposure came from TCDD by way of the food chain; silt runoff from sprayed areas into unsprayed waterways; some unrecorded U.S. or allied Agent Orange sprayings; inaccurately recorded sprayings; or sprayings whose wind drift was greater than 20 kilometers. Predictably, problems generated by the foregoing oversights, the mass of data to be analyzed as claims were filed, and the known loss of many service records would invalidate many veterans' legitimate claims.

Alternative 2:

Any Vietnam Veteran or child of a Vietnam Veteran who experiences a TCDD-like health effect shall be presumed to have a service-connected disability. This alternative is admittedly

broader than the first, and would provide benefits for some veterans who were not exposed to Agent Orange and whose disabilities are not presumably truly service-connected. Nevertheless, it is the only alternative that will not unfairly preclude receipt of benefits by a TCDD exposed Vietnam Veteran.

Furthermore, this alternative is consistent with the Secretary's decision regarding the service-connection of non-Hodgkin's lymphoma, as well as legal precedent with respect to other diseases presumed by the Department of Veterans Affairs to be connected to one or more factors related to military service (i.e. veterans exposed to atomic radiation and POW's with spastic colon).

PRESUMPTIONS OF AGENT ORANGE RELATED HEALTH EFFECTS

I have also given considerable thought to which health effects are to be presumed likelier than not to be related to TCDD exposure and therefore service-connected. Any such determination must be made in light of: 1) the review of the scientific literature, including animal studies where human data does not exist or has been manipulated; 2) the inappropriate processes of the Veterans Advisory Committee on Environmental Hazards; 3) the past political manipulations of Ranch Hand and CDC studies; and 4) the recent discoveries of manipulation by scientists hired by chemical manufacturers of dioxin contaminants to evaluate the potentially best epidemiological data concerning TCDD's effects on humans.

My evaluation of the evidence has been made with just such

considerations in mind. Additionally, I have conferred with several experts in the field. After evaluating all the evidence and material of record, I am convinced that there is better than "an approximate balance of positive and negative evidence" on a series of Agent Orange related health effects.

It can, in my judgment, be concluded, with a very high degree of confidence, that it is at least as likely as not that the following are caused in humans by exposure to TCDD: non-Hodgkin's lymphoma, chloracne and other skin disorders, lip cancer, bone cancer, soft tissue sarcoma, birth defects, skin cancer, lung cancer, porphyria cutanea tarda and other liver disorders, Hodgkin's disease, hematopoietic diseases, multiple myeloma, neurological defects and auto-immune diseases and disorders.

In addition, I am most comfortable in concluding that it is at least as likely as not that liver cancer, nasal/pharyngeal/esophageal cancers, leukemia, malignant melanoma, kidney cancer, testicular cancer, pancreatic cancer, stomach cancer, prostate cancer, colon cancer, brain cancer, psychosocial effects, and gastrointestinal disease are service-connected.

I have separated the two foregoing subsets subjectively only because there is somewhat more data to support the former than the latter. Nonetheless, immunological and toxicological theory supports both subsets and fully justifies, in my view, the inclusion of both subsets of the foregoing health effects in determining a service-connected injury.

Such a resolution of the embarrassingly prolonged Agent Orange controversy would be on the order of decisions to compensate U.S. soldiers who contracted cancer after exposure to radiation from atomic tests and U.S. soldiers involved, without their knowledge, in LSD experiments. With the scientific basis now available for it to be stated with confidence that it is at least as likely as not that various health effects are related to wartime exposure to Agent Orange, there is the opportunity finally to right a significant national wrong committed against our Vietnam Veterans.

RECOMMENDATIONS

1. That the Secretary undertake a prompt reevaluation of the compensation decision impacting on Vietnam Veterans exposed to Agent Orange in light of accumulating scientific evidence that discredits earlier "findings" of an insufficient linkage between dioxin contaminants in Agent Orange and rare disease, such as cancer illnesses.

2. To the extent that the Secretary deems it necessary to use the Veterans' Advisory Committee on Environmental Hazards to assist in his reevaluation, the current members should be dismissed -- having demonstrated a disturbing bias in their review to date of the scientific literature related to Agent Orange and dioxin -- and new members should be appointed in accordance with Section G of the Veterans' Dioxin and Radiation Exposure Compensation Standards Act, including persons with recognized scientific and medical expertise in fields pertinent

to understanding the health effects of exposure to dioxin. The Committee meeting currently scheduled for May 16th and May 17th should be cancelled.

3. That the Secretary in making his decision regarding Agent Orange compensation for Vietnam Veterans do so on the basis of his independent evaluation of the existing scientific and medical evidence on the health effects of exposure to dioxins, as cataloged and discussed in this Report, and in full recognition that the standard to be applied -- as mandated by both Congress and the courts -- requires the resolution of doubts as to a number of cancers linked to dioxins in favor of the Vietnam Veteran.

Union Calendar No. 415
101st Congress, 2d Session - - - - - - - - - - House Report 101-672

THE AGENT ORANGE COVERUP: A CASE OF FLAWED SCIENCE AND POLITICAL MANIPULATION

TWELFTH REPORT

BY THE

COMMITTEE ON GOVERNMENT OPERATIONS

together with

DISSENTING VIEWS

AUGUST 9, 1990.—Committed to the Committee of the Whole House on the State of the Union and ordered to be printed

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LETTER OF TRANSMITTAL

HOUSE OF REPRESENTATIVES,
Washington, DC, August 9, 1990.

Hon. THOMAS S. FOLEY,
Speaker of the House of Representatives,
Washington, DC.

DEAR MR. SPEAKER: By direction of the Committee on Government Operations, I submit herewith the committee's twelfth report to the 101st Congress. The committee's report is based on a study made by its Human Resources and Intergovernmental Relations Subcommittee.

JOHN CONYERS, Jr., *Chairman.*

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101ST CONGRESS, 2d Session | HOUSE OF REPRESENTATIVES | REPORT 101-672

THE AGENT ORANGE COVERUP: A CASE OF FLAWED SCIENCE AND POLITICAL MANIPULATION

AUGUST 9, 1990.—Committed to the Committee of the Whole House on the State of the Union and ordered to be printed

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Mr. CONYERS, from the Committee on Government Operations, submitted the following

TWELFTH REPORT

together with

DISSENTING VIEWS

BASED ON A STUDY BY THE HUMAN RESOURCES AND INTERGOVERNMENTAL RELATIONS SUBCOMMITTEE

On August 2, 1990, the Committee on Government Operations approved and adopted a report entitled "The Agent Orange Coverup: A Case of Flawed Science and Political Manipulation." The chairman was directed to transmit a copy to the Speaker of the House.

I. EXECUTIVE SUMMARY

The Human Resources and Intergovernmental Relations Subcommittee conducted a year-long investigation of the studies of Agent Orange exposure and Vietnam veterans' health conducted by the Centers for Disease Control (CDC) from 1982 to 1987. The exposure study was intended to be the first comprehensive effort by the Federal Government to determine the magnitude of Agent Orange exposure to U.S. military personnel serving in Vietnam during the war years. The separate health review is the largest medical study of Vietnam veterans undertaken by the Federal Government.

The subcommittee's investigation included an extensive review of documents related to the studies at the CDC Center for Environmental Health and Injury Control in Atlanta, Georgia, Interviews

were conducted of current and former CDC employees. The records of a White House panel, the Agent Orange Working Group (AOWG), were obtained from the U.S. National Archives and the Reagan Presidential Library, and reviewed by subcommittee staff. Interviews were also conducted of military records experts, epidemiologists, and environmental authorities employed by Federal agencies, veterans service organizations, and universities.

Agent Orange, so named for the orange stripe on the 55-gallon drums in which it was stored, was a herbicide used by the U.S. military during the Vietnam War to defoliate forests that concealed the activities of the enemy. It was a mixture of two chemical ingredients, the *n*-butyl esters of 2,4-D and 2,4,5-T. One of these chemicals, 2,4,5-T, contained 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. Known simply as dioxin, the chemical is considered one of the most toxic chemicals every created synthetically, and has proven to be carcinogenic in animal studies.

The study had been mandated by Congress more than a decade ago. The Veterans Health Programs Extension and Improvement Act of 1979 authorized the Veterans Administration (VA) to design and conduct a study to assess the exposure of Vietnam veterans to Agent Orange. In 1981, Congress enacted the Veterans Health Care, Training, and Small Business Loan Act, which expanded the scope of the VA study to include a health study of Vietnam veterans, using service during the war as an exposure factor, exposure to Agent Orange notwithstanding.

The CDC Agent Orange Exposure Study was canceled in 1987 when a White House panel, the AOWG, concluded that military records could not be used to assess exposure to the herbicide. The health status study was published in 1989, and a final study on selected cancers among Vietnam veterans was released in 1990.

The committee finds that the Agent Orange exposure study should not have been canceled because CDC did not document that exposure could not be assessed, nor did it explore alternative methods of determining exposure. The committee concludes that other methods of determining exposure were available to CDC, but intentionally disregarded.

The committee's report concludes that the CDC study was changed from its original format so that it would have been unlikely for the soldiers who received the heaviest exposure to the herbicide to be identified. CDC accomplished this by unjustifiably discrediting the military records provided to it by the Department of Defense's Environmental Study Group (ESG). The key alteration was CDC's decision to track troop movements using broad battalion records, which are less precise than the company-level records the Agency had originally intended to use to follow troop positions during the Vietnam War.

After restricting the study by eliminating thousands of veterans who would have been most likely to have been exposed to Agent Orange, CDC attempted to validate its flawed exposure definitions with a test to identify traces of dioxin in the blood of the veterans who had been studied. When the blood test failed to find elevated levels of dioxin in the veterans' blood, the White House instructed CDC to halt the study. The committee found that the blood test was based on flawed and manipulated estimates of the ability of

dioxin to remain in human blood 20 years after exposure. The weight of scientific evidence indicates that dioxin cannot be traced in all veterans who were exposed to Agent Orange two decades ago.

The committee also concludes that the CDC study was controlled and obstructed by the White House, primarily through its AOWG and the Office of Management and Budget (OMB), because the Reagan administration had adopted a legal strategy of refusing liability in military and civilian cases of contamination involving toxic chemicals and nuclear radiation.

The report's final conclusion is that the Federal Government has suppressed or minimized findings of ill health effects among Vietnam veterans that could be linked to Agent Orange exposure. Federal studies have found that Vietnam veterans are more susceptible to diseases such as non-Hodgkin's lymphoma and soft tissue sarcoma. Studies have also concluded that the offspring of Vietnam veterans suffer higher incidences of certain birth defects, such as cerebrospinal malformations, and that Vietnam veterans have sperm malformations and low sperm counts. The Federal Government has consistently refused to acknowledge any link between these diseases and Agent Orange, even though the maladies are known consequences of herbicide exposure in the civilian workplace.

The committee recommends that Congress mandate the creation of an accurate Agent Orange exposure index, and that the index be used, through a contract to a private organization, to conduct an independent epidemiological study of the effects of the herbicide on Vietnam veterans. The committee also recommends that the White House be barred from interfering with all Federal scientific research.

II. Introduction

Under the House of Representatives' Rule X, 2(b)(2), the Committee on Government Operations is authorized to "review and study, on a continuing basis, the operation of Government activities at all levels with a view to determining their economy and efficiency." The committee has assigned this responsibility, as it pertains to the Department of Health and Human Services (HHS) and, its component, the Centers for Disease Control (CDC), to the Human Resources and Intergovernmental Relations Subcommittee.

Pursuant to its authority, the subcommittee conducted a two-year investigation of the studies of Agent Orange exposure and Vietnam veterans' health conducted by CDC from 1982 to 1987 and other studies of herbicides as a cause of disease. The exposure study was intended to be the first comprehensive effort by the Federal Government to determine the magnitude of Agent Orange exposure to U.S. military personnel serving in Vietnam during the war years. The separate health review is the largest medical study of Vietnam veterans undertaken by the Federal Government.

The subcommittee's investigation included an extensive review of documents related to the two studies at the CDC Center for Environmental Health and Injury Control in Atlanta, Georgia. Interviews were conducted of current and former CDC employees who worked on the studies. The records of a White House panel, the

Agent Orange Working Group (AOWG), were obtained from the U.S. National Archives and the Reagan Presidential Library, and reviewed by subcommittee staff. Interviews were also conducted of military records experts, epidemiologists, and environmental authorities employed by Federal agencies, veterans service organizations, and universities.

The subcommittee's investigation included two public hearings, which were conducted on July 11, 1989,[1] and June 26, 1990.[2] The following witnesses testified at the first hearing: Honorable Lane Evans, a Representative in Congress from the State of Illinois; Lawrence B. Hobson, M.D., Ph.D., Director, Office of Environmental Medicine, Department of Veterans' Affairs, accompanied by Donald Ivers, acting general counsel, and Fred Conway, special assistant to the general counsel; Vernon N. Houk, M.D., Director, Center for Environmental Health and Injury Control, Centers for Disease Control; Michael Kafrissen, M.D., former medical epidemiologist, Centers for Disease Control; Philip J. Landrigan, M.D., director, Division of Environmental and Occupational Medicine, Mount Sinai School of Medicine; Ellen K. Silbergeld, Ph.D., director, Toxic Chemicals Program, Environmental Defense Fund; Dennis M. Smith, M.D., former visiting scientist, Centers for Disease Control; John F. Sommer, Jr., director, National Veterans Affairs and Rehabilitation Commission, the American Legion; Jeanne M. Stellman, Ph.D., epidemiologist, American Cancer Society; Steven D. Stellman, Ph.D., Assistant Commissioner for Biostatistics and Epidemiologic Research for the Department of Health of the city of New York; and Mary R. Stout, president, Vietnam veterans of America.

The following witnesses testified at the second hearing: Richard W. Clapp, M.P.H., Sc.D., director, Environmental Health Studies, JSI Research and Training Institute; Peter C. Kahn, Ph.D., Associate Professor of Biochemistry, Rutgers University; Arnold Schecter, M.D., M.P.H., Professor of Preventative Medicine, State University of New York Health Science Center; Ellen K. Silbergeld, Ph.D., senior scientist, Environmental Defense Fund; Daniel Thou Teitelbaum, M.D., president, Medical Toxicology Partnership; Shelia Hoar Zahm, Sc.D., epidemiologist, National Cancer Institute; and Admiral Elmo R. Zumwalt, Jr., USN Ret., Special Assistant to the Secretary of Veterans Affairs.

III. Background

Agent Orange, so named for the orange stripe on the 55-gallon drums in which it was stored, was a herbicide used by the U.S. military during the Vietnam War to defoliate forests that concealed the activities of the enemy. It was a mixture of two chemical ingredients, the *n*-butyl esters of 2,4-D and 2,4,5-T. One of these chemicals, 2,4,5-T, contained 2,3,7,8-tetrachlorodibenzo-*p*-dioxin.

[1] Hearing before a subcommittee of the Committee on Government Operations, U.S. House of Representatives, "Oversight Review of CDC's Agent Orange Study," July 11, 1989, hereinafter referred to as "Hearing, 1989."

[2] Hearing before a subcommittee of the Committee on Government Operations, U.S. House of Representatives, "Links Between Agent Orange and Other Herbicides With Diseases," June 26, 1990, hereinafter referred to as "Hearing, 1990."

Known simply as dioxin, the chemical is considered one of the most toxic chemicals ever created synthetically, and has proven to be carcinogenic in animal studies.

According to the Office of Environmental Medicine in the Department of Veterans' Affairs, 15 different herbicides were used in Vietnam between January 1962 and September 1971. More than 80 percent of the defoliation operations used Agent Orange, which was sprayed primarily between January 1965 and April 1970. Among the other herbicides used prominently were Agent White, which also contained 2,4-D, and Agent Blue, which consisted of an organic arsenic compound called cacodylic acid. Less than 7 percent of the total acreage sprayed during the Vietnam War was covered prior to 1965. Most of the spraying occurred from 1966 to 1969. Overall, more than 20 million gallons of herbicides were sprayed upon 6 million acres. More than 3.5 million acres were sprayed more than once.

Herbicides were used for three main purposes during the Vietnam War. The principal uses were to defoliate military areas to improve observation, and to destroy crops to diminish the enemy's food supply. A third purpose was to clear vegetation around fire bases and such installations, around landing zones, and along lines of communication. Herbicide usage began in 1962, was expanded in 1965 and 1966, and peaked from 1967 to 1969. Herbicides were phased out in 1970 when it was learned that mice exposed to the chemical components of the herbicides bore offspring with birth defects.

Most of the herbicides were sprayed from fixed-wing aircraft in a project called, "Operation Ranch Hand." But herbicides were also sprayed from helicopters, trucks, riverboats, and hand applicators.

Spraying occurred in all military zones of Vietnam. The most heavily sprayed areas included inland forests near the demarcation zone, inland forests at the junction of the borders of Cambodia, Laos, and South Vietnam, inland forests north and northwest of Saigon, mangrove forests on the southern-most peninsula of Vietnam, and mangrove forests along major shipping channels southeast of Saigon. Crop destruction missions were concentrated in northern and eastern central areas of South Vietnam.

Many Vietnam veterans believe their exposure to Agent Orange has caused a variety of ailments, including cancer, birth defects, and emotional disorders linked to neurological dysfunction. Their concerns are heightened by what science has discovered about the possible effects of dioxin exposure but, also, by what is not known about the chemical's effects on humans.

Dioxin is the useless, unwanted byproduct from the production and use of chlorinated phenols. Environmental hazards have also been caused by toxic compounds related to dioxin, such as polychlorinated biphenyls (PCB's), polybrominated biphenyls (PBB's), polychlorinated dibenzofurans (PCDF's), polychlorinated naphthalenes, and polychlorinated terphenyls.

Dioxin is omnipresent, existing in household products, dust particles, and water. It has been found in significant levels across the world. Millions of people have been exposed to it through industrial accidents, fly ash from waste incinerators, herbicide spraying, manufacturing plants, and even in some edible fish.

There is no disagreement among scientists that dioxin in its pure form is the most toxic synthetic chemical in existence. Fortunately, humans are never exposed to undiluted amounts of the substance. It occurs as trace quantities in the ranges of parts per billion or parts per million as a contaminant in other products. Sometimes—in the case of fish, for example—it occurs in parts per trillion, or, in the case of water, parts per quadrillion.

Animal experiments have found dioxin toxicity to be dose-related. At low doses, there are no observed toxic effects of dioxin in animals. However, in high doses, various species have developed such diseases as hepatic necrosis and T-cell depression. Increased incidences of cancer were observed in most species exposed to dioxin during laboratory experiments.

Corresponding dose-related research cannot be legally or morally conducted on humans. However, there is some limited information about the effects of dioxin on humans as a result of inadvertent exposure from industrial accidents. A recent accident occurred in Seveso, Italy, when a cloud of trichlorophenol and dioxin spread over seven square miles of populated territory. In another accident, transformer fluid was inadvertently mixed with rice oil, affecting seven thousand people who ingested the toxic oil in Japan and Taiwan. Similar accidents occurred in West Virginia, New Jersey, and England. The most severe accidents to date occurred in West Germany and Czechoslovakia. The most well-known dioxin incidents in the United States probably were the Times Beach, Missouri, and Love Canal, NY, disasters, when dioxin from an industrial plant had seeped into the soil of residential communities.

The most serious health consequences of these accidents were neuropathy and liver damage in approximately one-third of the victims of the incidents in West Germany and Czechoslovakia. There were similar consequences of the West Virginia and New Jersey accidents. The most prevalent reaction to dioxin contamination—which may be a marker of exposure and a warning sign for disease that can take decades to develop—is the skin condition, chloracne, a painful and extremely annoying ailment, but not life threatening. Chloracne has occurred in workers and residents exposed during most industrial accidents where high levels of dioxin were released.

Some studies of industrial accidents involving dioxin have found incidences of soft tissue sarcoma, a rare form of cancer, in those exposed to the chemicals, but some in the scientific establishment consider the numbers of study subjects too small to carry the weight of significance. The U.S. Centers for Disease Control, in a recent study of Vietnam veterans, found that veterans who had served in Vietnam had significantly higher incidences of non-Hodgkin's lymphoma, another rare illness, but dismissed any possible connection to Agent Orange exposure, instead claiming it did not know why the veterans had higher levels of the disease. In March 1990, the CDC report prompted the Department of Veterans' Affairs to declare non-Hodgkin's lymphoma a monetarily compensable, service-connected disease, but the Department did not link the illness to Agent Orange exposure. In May 1990, the Department also declared soft-tissue sarcoma, a rare cancer, to be a service-connected, compensable malady for Vietnam veterans on the basis of a

report by the Department's Veterans Advisory Committee on Environmental Hazards, which found that herbicides may have caused the disease.

The rationale behind the U.S. Government's refusal to accept any causal effects between Agent Orange and all but a few diseases stems from the CDC exposure study, which was canceled when the Agency declared such a study to be scientifically impossible.

The study had been mandated by Congress more than a decade ago. The Veterans Health Programs Extension and Improvement Act of 1979 authorized the Veterans Administration (VA) to design and conduct a study to assess the exposure of Vietnam veterans to Agent Orange. In 1981, Congress enacted the Veterans Health Care, Training, and Small Business Loan Act, which expanded the scope of the VA study to include a health study of Vietnam veterans, using service during the war as an exposure factor, exposure to Agent Orange notwithstanding.

The VA's efforts to conduct the study were mired in delays. In 1982, three years after passage of the Agent Orange study legislation, the agency had not even begun the study. The House and Senate Veterans Affairs Committees decided to transfer the study from the VA to the CDC, after the Director of the CDC Center for Environmental Health and Injury Control testified at a hearing that CDC could do the study better and faster than the VA. Less than a year later, Congress passed an appropriations bill containing $54 million, to be provided through the VA's budget, for CDC to conduct the Agent Orange study. Approximately $43 million of the appropriated funds were expended before the study was canceled.

CDC, like the VA before it, had two missions. One, to design and implement a study to measure the exposure of Vietnam veterans to Agent Orange, and the second to assess the overall health of Vietnam veterans. The latter mission was divided into two studies. The first study involved conducting physical examinations of the subjects and reviewing their medical records. The second part was a study of the incidence of selected cancers among Vietnam veterans.

In January 1989, CDC published the results of the separate health assessment, called the Vietnam Experience Study (VES), in five volumes. CDC claimed the study found little differences between the two cohorts involved: veterans who served in Vietnam and veterans who did not during the same time period. In early 1990, CDC published the Selected Cancers Study, which found that Vietnam veterans were at greater risk of one cancer, non-Hodgkin's lymphoma.

The exposure study was intended to be a landmark review. For the first time, formal scientific research would be conducted to determine which soldiers were in areas sprayed with Agent Orange. The exposure assessment study was canceled in September 1987, after the White House AOWG contended that it was scientifically impossible to assess the exposure of Vietnam veterans to Agent Orange due to the inadequacy of military records. The first and only attempt by the Federal Government to determine the exposure to Agent Orange by U.S. military personnel never reached a conclusion, other than that the study was impossible to do. The question foremost in the minds of Vietnam veterans and the Congress in regard to Agent Orange has still not been answered.

IV. Findings

A. THE CDC AGENT ORANGE EXPOSURE STUDY SHOULD NOT HAVE BEEN CANCELED BECAUSE IT DID NOT DOCUMENT THAT EXPOSURE OF VETERANS TO THE HERBICIDE COULD NOT BE ASSESSED, NOR DID CDC EXPLORE ALTERNATIVE METHODS OF DETERMINING EXPOSURE

In its November 1987 final report, *Comparison of Serum Levels of 2,3,7,8-TCDD With Indirect Estimates of Agent Orange Exposure in Vietnam veterans*, the CDC concluded:

> The findings of this study and the conclusions from the AOWG [Agent Orange Working Group of the White House] Science Sub-Panel report on exposure assessment * * * do not identify any method for utilizing military records or self-reported exposure to distinguish between U.S. Army ground combat troops who were and were not exposed to Agent Orange in Vietnam, as would be needed for a cohort study of possible health effects.[3]

This conclusion was used as the basis by the White House and CDC to cancel the study and end all Federal attempts to study the link between Agent Orange and the health problems of Vietnam veterans.[4]

The law directing the U.S. Government to assess the exposure of veterans to Agent Orange was not specific about the method of study, only that a study be conducted. The final protocol for the study was left to the discretion of CDC, with the Congressional Office of Technology Assessment (OTA) and the Institute of Medicine (IOM) serving as peer reviewers. CDC could only abandon the study if no method to assess exposure could be identified ot all. CDC reached just such a conclusion. The study was canceled when CDC and the White House Panel decided that no methods of any kind existed to use military records to distinguish between exposed and unexposed soldiers who served in Vietnam.

The subcommittee's investigation of the CDC study has established that other methods existed to assess exposure of veterans to Agent Orange. Therefore, CDC erred when it reported that it could not identify any method of determining exposure. Evidence compiled by the subcommittee demonstrates that other methods were available, but were ignored or dismissed by CDC.

CDC's mistake was described by Dr. Philip J. Landrigan, one of the foremost epidemiologists in the United States, who stated that the Agency had ignored a large group of veterans who had been potentially exposed to Agent Orange. He testified that the attempt to determine Agent Orange exposure in Vietnam veterans was analogous to an earlier effort by CDC to determine exposure to

[3] "Comparison of Serum Levels of 2,3,7,8-TCDD With Indirect Estimates of Agent Orange Exposure in Vietnam veterans," Final Report, Agent Orange Projects, Division of Chronic Disease Control, Center for Environmental Health and Injury Control, Centers for Disease Control, Public Health Service, U.S Department of Health and Human Services, November 1987, pp 4-5

[4] Hearing, 1989, pp 55-57 Letter from James O Mason, M D., Dr P H., Assistant Surgeon General, Director, Centers for Disease Control, to Don Newman, Chair, Domestic Policy Council Agent Orange Working Group, October 28, 1987.

PBB, a toxic chemical related to dioxin, following an industrial accident in Michigan.

> In response to the disaster, just as in response to the Agent Orange episode in Vietnam, a series of epidemiologic studies were undertaken. The first of these studies was an investigation that was undertaken by our group at CDC in which I was the coprincipal investigator. . . .
>
> We conducted a survey in which we did physical examinations, took blood samples on a very carefully targeted list of people in Michigan who we identified through records of contaminated farms. In theses populations of people who were very carefully targeted, we found a very high proportion who had elevated serum levels of PBB. Their levels were roughly in proportion to the extent of their exposure.
>
> At about the same time Dr. Irving Selikoff . . . took this group into Michigan and did a statewide survey to determine the proportion of people in Michigan who had been exposed to PBB. He found . . . that only a small proportion of the people whom he tested had elevated serum levels of PBB.
>
> Now, Dr. Selikoff could have said on the basis of those findings that most residents of Michigan are not exposed to PBB and that statewide records do not constitute a good basis for identifying people in Michigan who have been exposed to this toxic compound. In other words, he could have drawn conclusions that would have been parallel in their content to the conclusions that CDC drew with regard to the exposure to dioxin in Vietnam.
>
> He didn't do that, though. He recognized the possibility that there might exist a heavily exposed subgroup within the population. . . . and he urged the need for further research. And, in fact that research still continues today.
>
> . . . . . .
>
> I think the analogy is obvious and I think the question that confronts us today . . . is the question of whether there might exist within the population of millions of soldiers and marines and sailors and Air Force men who went to Vietnam a heavily exposed subgroup comprising maybe 5 percent, maybe 10 percent of the total, who were heavily exposed. There are several lines of evidence which suggest that such groups exist.[5]

In its final report, CDC contended that available military record regarding troop movements and the spraying of Agent Orang were insufficient to identify veterans who had been exposed to th defoliant; the purported inadequacy of the military records was th primary reason the exposure study was canceled and termed in possible to complete. The final CDC report stated:

[5] Hearing, 1989 Testimony of Philip J Landrigan, M D., Director, Division of Environment and Occupational Medicine, Mount Sinai School of Medicine, New York, NY, pp 221-223

> . . . At best, available military data permit only a probabilistic assessment of *opportunity* for exposure. Accurate individual exposures to Agent Orange cannot be determined because there is limited knowledge about the initial dispersion, biodegradation, and eventual ecologic disposition of Agent Orange in Vietnam; uncertainty about the absorption of Agent Orange or TCDD in humans; and the inability to determine the precise location of individual soldiers in relation to Agent Orange applications. Because of these uncertainties, the November 1983 protocol for the Agent Orange Study indicated that further pilot testing would be needed before a decision could be made to proceed with the full-scale study. . . . military records alone could not be used to estimate possible exposure of individual men to Agent Orange. In addition, some reviewers were concerned that too few men were identified as having "meaningfully high" exposure opportunity scores to warrant proceeding with a full-scale study.[6]

The CDC conclusion that military records could not be used to identify exposed veterans has been disputed by former CDC scientists, Department of Defense records experts, and prominent private sector epidemiologists.

Dr. Jeanne Stellman of Columbia University, who conducted an epidemiologic study for the American Legion, testified before the subcommittee that available records were quite sufficient to determine exposure to Agent Orange.

> . . . We are talking about 11,197,929 gallons sprayed on Vietnam that we know the locations of pretty well. In addition, Richard Christian's [7] group then picked up an additional 13 percent of what is now the total . . . tape records of 1,593,380 gallons of herbicides given off by fixed-wing aircraft, helicopters, and ground equipment such as backpacks, and something that everybody's always referring to [as] the unknown sources, but which, in fact, only represents 20,000 gallons.
>
> So this data that you heard being disregarded and tossed out as useless to evaluate veteran's health and well-being, in fact, is the tape that was developed and used by the National Academy of Sciences . . . we have here data on more gallonage and more usage of herbicides than I would say that we have in anyplace else including all the usage in the United States which we don't have a good handle on.[8]

Dr. Dennis Smith, a scientist who worked on the CDC Agent Orange Project, was one of the people responsible for evaluating records provided to CDC by the Department of Defense. He testified that the CDC staff had developed numerous alternatives to the approach the agency used to assess exposure, and that he and others at CDC believed sufficient information existed to compensate for gaps in the military records transmitted by the Pentagon. But, he testified, his superiors were resistant to exploring the alternatives.

> We didn't really inform people what we were doing. We should have publicized it to a greater extent and gotten more feedback on it. We had tremendous problems with developing exposure indices but they were not in creating new indices. We had many new indices and many different things to try and experiment with. But, we had problems in selling these indices to our superiors and people at the Office of Technology Assessment.[9]

Smith also testified that he believed CDC officials blamed certain gaps of information in the military records to cover up the problems CDC was having in identifying dioxin in the bodies of Vietnam veterans.

> Considerable concern arose over the scientific problems that plagued the Agent Orange Study, and an attempt was made to divert focus from these methodological issues to other areas that had origin or direction outside of Centers for Disease Control. The first, and most useful diversion, was to the fact that improper location data would destroy the usefulness of the exposure index. Regardless of any utility the data might have, if it was not "complete" (i.e. a troop location for every single unit on every single day) then it would be the troop location data that introduced the major error into the exposure index. Previous concepts of gap-filling, imputation, verification of troop locations, obtaining locations from other sources, etc. were no longer valid; the utility contained in the data already available from ESG [Environmental Support Group of the Defense Department] was ignored, and concepts developed that initially supported the data, such as "digit preference," were now directed against the ESG data.[10]

At one point during the performance of the study, Dr. Smith sought data from outside the Environmental Support Group to buttress the military records already obtained by CDC. On May 14, 1985, he sent a memorandum to the Chief Scientist of the CDC Agent Orange Project, detailing a visit to the Military History Institute and U.S. Army War College in Carlisle, Pennsylvania.

> . . . The historical records available at Carlisle appear to be of tremendous importance to our Agent Orange Projects in respect to several aspects of our interest in the Southeast Asia conflict. To wit: (1) Troop location; (2) Herbicide Missions; (3) Medical Information; (4) Possible models of troop movement; (5) Computer operations used during the time period of interest. The records provide expanded knowledge on these areas and help facilitate an understanding of the situations in Southeast Asia that

[6] Op cit., p. 9. See footnote 3.
[7] Richard Christian directed the Department of Defense's Environmental Support Group, which supplied Agent Orange spray records and military troop movement records to CDC.
[8] Hearing, 1989, p. 158.

[9] Ibid. Testimony of Dennis M. Smith, M.D., former visiting scientist, Centers for Disease Control, p. 80.
[10] Ibid., pp. 93-94.

might affect our projects. These records are great in number and generally are not indexed: researching a particular subject may be quite time-consuming, but in my "clinical impression," may be generally productive.[11]

In 1985, officials at the Defense Department's ESG discovered that CDC was disputing the accuracy of the military records. The ESG Chief of the CDC Support Branch, who was responsible for transmitting the records to CDC, warned that CDC did not understand how to use the records and appeared to be ignoring ESG's advice. The Chief noted that gaps in military tracking records could be filled with supplementary documents, such as company morning reports. In a memorandum to the Director of ESG, the CDC Support Branch Chief described how CDC had disputed, without justification, some records provided by ESG. Quoting from a CDC internal report, the Chief wrote:

> . . . ESG claimed that additional documents exist that might help place companies on a daily basis. ESG has not *claimed* anything, this statement is fact. Who are these experts who make decisions based on a computer distance comparison? For instance, the example CDC gives for Cu Chi taken from the morning reports substantiates the accuracy of the APO's that are listed. The grid coordinate and the APO number show the location as Cu Chi. What evidence does CDC have that indicates this unit was not at Cu Chi? This information was taken from official Army archival records. It must be stated for the record, that a morning report is a company document not a brigade or division record.[12]

The memorandum also expressed concerns that CDC was ignoring ESG's advice and preparing its own, incorrect, analyses of the military records. For example, CDC had dismissed the use of company morning reports to fill in missing locations in the main data base.

The ESG memorandum states:

> . . . Our main concern is that CDC does not keep ESG advised on these types of analysis until after the fact. Our expertise is U.S. Army combat unit records and troop movements, yet we have no idea if the proper grid coordinate locations were being compared. We feel a more detailed analysis needs to be performed on this information before a decision is made not to use morning report data.[13]

Richard Christian, who directed the ESG during the CDC study, testified that he had informed CDC on numerous occasions that records were available to address all of CDC's concerns about gaps

[11] "Site Visit Summary, Carlisle Barracks Military History Institute and US Army War College," Memorandum from Dennis M. Smith, M.D., visiting scientist, Centers for Disease Control, to Daniel L. McGee, Ph.D., Chief Scientist, Agent Orange Projects, Centers for Disease Control, May 14, 1985, p. 1.

[12] "Centers for Disease Control Report to OTA," Memorandum for the Director from Donald C. Hakenson, Chief, CDC Support Branch, Department of the Army, U.S. Army and Joint Services Environmental Support Group, October 25, 1985, p. 1.

[13] Ibid., p. 2.

in the data base. Yet, CDC reported to OTA that sufficient records were not available to complete the exposure study. Christian testified:

> . . . I was investigated by the National Academy of Sciences on two occasions. The Science Panel of the White House Agent Orange Working Group was at my office numerous times. There were visits from the OTA to look at these records and it's just inconceivable to us and to the Environmental Support Group that they could say that these records were not adequate to do an Agent Orange study.[14]

Christian's testimony raised questions about the ability of the CDC staff to sufficiently comprehend and use the military records. He testified about being astounded when he discovered that CDC was identifying enemy locations when it thought it had pinpointed U.S. sites.

> At one point, the Centers for Disease Control attempted to take over the work of ESG from the study. My staff provided the CDC with copies of daily journals. In a test of that exercise, the personnel in the Centers for Disease Control recorded the grid points from the Viet Cong locations. Certainly we were not interested in the enemy locations; we were looking for the U.S. locations and the U.S. grid points.[15]

In an interim report in 1985, CDC claimed that the ESG had not provided gap-filling information, such as morning reports. Christian testified that the interim report was false.

> . . . If we traced the record of the Environmental Support Group back to 1981, I reported to Congress that there were several collections of records that would provide company information beginning with daily journals, operational reports of lessons learned, command reports, situation reports, intelligence reports, and morning reports.
>
> Yet in that interim report No. 2 . . . they indicate . . . that I didn't tell them about morning reports. Well, I don't know what else I could have done, with testifying before Congress four times, preparing a report at the International Dioxin Conference, laying out all of those types of records with 27 meetings with the VA before the CDC took over.
>
> Certainly everyone was aware of those collections.[16]

As the study ensued, the limitations in the methodology chosen by CDC prevented the Agency from identifying Vietnam veterans exposed to Agent Orange. A further constraint on the outcome was CDC's decision to use but one approach to identify exposed veterans when others existed.

[14] Hearing, 1989 Testimony of Richard Christian, former Director of the U.S. Army and Joint Services Environmental Support Group, Department of the Army, pp. 42-43.

[15] Ibid., p. 42.

[16] Ibid., p. 41.

The committee believes that the decision by the White House to cancel the Agent Orange study was premature, and failed to give the Agency the opportunity to explore alternative methodologies. The justification for cancelling the studies—that military records alone could not be used to conduct an Agent Orange exposure study—was misleading. Clearly, better alternatives had not been fully considered before the study was canceled.

In particular, CDC did not attempt to identify the group of veterans described in Dr. Landrigan's testimony as being highly exposed. The Government was aware of situations where soldiers had been highly exposed, but this information was not considered by CDC. For example, a highly exposed group of veterans was discovered by the White House in 1981. According to a White House memorandum:

> Newly reviewed data shows that a plane taking off from the Bien Hoa Base in Vietnam on a date certain, discovered a faulty engine, turned left to go back to the air-strip, and promptly dumped 500 gallons of Agent Orange on the base camp from a height of 2,000 feet: the "dump value rate" of the plane used was 1,000 gallons in 30 seconds and suggests a high exposure to Agent Orange by a newly defined but as yet unidentified population.[17]

The memorandum states that files in the Office of the Army Adjutant General showed that there were 87 such aborted defoliating missions in Vietnam, and that 41 of the missions involved Agent Orange.[18] The White House was aware of the missions and their locations, yet CDC did not attempt to include the unknowing veterans who received these highly-concentrated exposures in its study.

8. THE ORIGINAL PROTOCOL FOR THE CDC AGENT ORANGE STUDY WAS CHANGED TO THE POINT THAT IT WAS UNLIKELY FOR THE HEAVIEST EXPOSED SOLDIERS TO BE IDENTIFIED

It is important to remember that the Agent Orange exposure assessment study was designed to identify soldiers who were exposed to the herbicide, not to link disease to exposure. That would have come later had the study not been canceled. The only records available to CDC were the troop movement records and the Agent Orange spray data in the files of the Department of Defense. Therefore, CDC had to design the best method of using troop location information to match against the spray records.

But from the start, CDC disregarded the records of soldiers who would have been among the most likely to have been exposed. The original protocol for the CDC Agent Orange Study contained numerous restrictions which would have the effect of arbitrarily limiting the number and type of veterans selected for the study. The protocol states:

> CDC proposes to limit this study to draftees and single-term enlistees in the non-officer ranks who served in the Army (grades E1 through E5 only); selection will be further limited to those who had only one tour of duty in Vietnam. Exclusion of officers is based primarily on a desire to make the groups as homogeneous as possible with respect to pre-existing demographic factors which could influence health. In addition, the inclusion of officers might require substantially increased record review to assess herbicide exposure potential . . . because of multiple tours of duty in Vietnam.[19]

[17] "New Information Regarding Agent Orange," The White House, Memorandum from Shannon Fairbanks to Martin Anderson, September 9, 1981, p. 1.
[18] Ibid.

CDC eliminated from the study all military service branches other than the Army. It excluded all officers and anyone who served more than one tour of duty in Vietnam. The reason for these exclusions was to reduce the amount of record review. Clearly only a small percentage of available records were reviewed by CDC.

The study group selection was also limited only to veterans serving in III Corps, thus eliminating six other combat corps stationed in Vietnam during the war.[20] The study group was also limited to the time period, 1967 to 1968.[21]

Importantly, the original protocol called for soldiers to be tracked according to company records because the data is the most precise and also because companies were the smallest units for which data was available. The use of company records would have enabled CDC to track individual soldiers. CDC recognized the importance of company records and was aware early on that the records could be incomplete. Still, the Agency's scientists believed the problem could be surmounted. CDC stated in the original protocol "that it is not necessarily wise to exclude a unit simply because some of its records are missing—units with missing records could have had more or less exposure to herbicides than units with complete records."[22]

The protocol reveals that the limitations in subject selection are due to expediency, particularly to prevent lengthy record reviews. For example, in deciding to exclude Marines from the study group, the protocol states:

> The desire to omit the Marine Corps from this study can now be more easily understood. If Marines were included, the records review and other selection tasks to this point would have to be done separately for them because they were largely stationed in 1 Corps, and this would cause delay.[23]

The original protocol documents that CDC intended to look only at a small portion of the records available, not because the data was unusable, but because Agency officials thought looking at all the records would require too much time. Yet, based on only a limited review of available records, the study was canceled in the end because CDC found military records could not be used to identify

[19] "Protocol for Epidemiologic Studies of the Health of Vietnam veterans," Centers for Disease Control, Public Health Service, U.S. Department of Health and Human Services, November 1983, p. 10.
[20] Ibid., p. 11
[21] Ibid., p. 12.
[22] Ibid.
[23] Ibid., p. 14

veterans who had been exposed to Agent Orange. The committee questions CDC's conclusion that the records could not be used because CDC did not consider all the records.

The protocol also suggests that the study would have certain limitations beyond the restrictions CDC had placed on the subjects to be selected for cohorts. "Unavoidable limitations of the proposed studies, or indeed any other studies which could be done, will preclude describing the results as 'definitive'" the protocol cautioned.[24] The protocol stated that one important limitation was the observational, as opposed to experimental, nature of the study.

> . . . Another general caveat is that it is not possible to prove a negative—that is, it will never be possible to say with certainty that herbicide exposure or some other factor connected with Vietnam service did not cause any adverse health effects.
>
> • • • • •
>
> . . . Moreover, even in the absence of exposure misclassification, the studies will have low power for rare diseases and/or low increases in risk, or for increases in risk limited to those veterans with prolonged and/or heavy exposure to herbicides or some other harmful factor. Thus, an overall finding of no increase in risk might "hide" a real increase for specific disease categories or special groups of veterans.[25]

After preparing the original protocol, with all its limitations and caveats, CDC diluted the study even further by adding more restrictions to the criteria for the inclusion of subjects. A February 1985 internal, interim report reveals that CDC made four major modifications in the original protocol. The most serious modification was that:

> . . . Battalions—rather than companies—will serve as the basis for cohort selection and unit location.
>
> • • • • •
>
> . . . Current data indicate that daily location information is not consistently available for units smaller than battalions. In other words, we believe that the location of individual battalions can be placed with reasonable accuracy for most of the 731 days but the locations of the component companies of a battalion cannot be as reliably placed due to lack of data.[26]

The effect of this change would be to severely diminish the study's ability to identify veterans most likely to have been exposed to Agent Orange. The interim report admits as much. ". . . because battalions are larger, more dispersed units than companies, the location of men in relation to herbicide applications will be known with less precision than envisioned in the protocol." [27]

[24] Ibid., p. 37.
[25] Ibid.
[26] "Agent Orange Projects Interim Report. Agent Orange Study Exposure Assessment. Procedures and Statistical Issues," Agent Orange Projects, Center for Environmental Health, Centers for Disease Control, February 1985, p. 4
[27] Ibid., p. 1.

CDC's decision to use battalion data was based on its conclusion that the military records were not accurate for the purpose of tracking companies. OTA concurred in this decision at the time. However, as noted previously, testimony and documents provided to the subcommittee indicate that CDC's decision was disputed, not only by the Department of Defense, which had greater expertise in evaluating military records, but by scientists working on the Agent Orange Project itself.

The second major change in the protocol was that the ". . . Ranking of unit exposure likelihoods will not determine selection of men into the study." [28] Originally, CDC planned to rank 125 companies according to time and distance proximity to herbicide applications, before any individuals from the units were selected for the study. The interim report states this approach was abandoned because CDC had identified numerous transfers of soldiers between companies in III Corps.[29] Therefore, unit exposures would not necessarily correlate to individual exposures.

The committee finds this change to be another example of CDC's dilution of the study for reasons of convenience and expedience. The individual soldiers could have been tracked, adjustments made for transfers, but because of the amount of time and work involved, and due to its own perception that the study had to be completed post-haste, this more precise method of tracking individual companies and soldiers was disregarded. The committee recognizes that pursuing alternatives would have been a complicated and arduous task; however, it was feasible. Because CDC diluted the study without doing the necessary work to compensate for tracking problems, the committee finds no support for the final conclusion that the Agency could not identify any method for using military records to assess exposure.

The interim report discussed two additional changes in the original protocol: Individual military records would be used to buttress unit morning reports to track troop movements and the study would be restricted to men serving only in infantry or artillery units. In explaining the reason for the latter alteration, CDC revealed that many soldiers likely to have been exposed were arbitrarily eliminated from the study because their backgrounds might not conform to the backgrounds of the study comparison group who did not serve in Vietnam. According to the interim report:

> . . . For the Agent Orange Study, our goal is not to select a "representative" sample of Army men in III Corps, but rather to select men from III Corps who are as *comparable* as possible, except for differing likelihoods of Agent Orange exposure. We believe that men serving in artillery and infantry battalions will resemble each other more closely in terms of baseline characteristics and general military experience than they would resemble men from cavalry, armor, and engineering units.[30]

[28] Ibid., p. 6
[29] Ibid
[30] Ibid., p. 9

The effect of these modifications on the study was noted in the interim report.

> . . . because unit exposure likelihoods do not appear to correlate highly with individual men's exposure likelihoods, wa will not be able to exclude men from units with intermediate exposura likelihoods from the study; therefore the spread or range of exposure likelihoods between the groups being compared will likely be reduced.[31]
>
> [Further,] The misclassification of Agent Orange exposure inherent in this study means that the true magnitude of exposure-disease associations will be underestimated.[32]

By the end of 1985, CDC scientists realized that the restrictions in the criteria described previously had so limited the scope of their research, they were unable to identify enough subjects for inclusion in the study. To compensate, CDC changed the criteria again, allowing a larger number of soldiers to be included, but reducing the numbers of soldiers with the greatest likelihood of exposure to Agent Orange. On December 8, 1985, new criteria were established in a second, interim report.[33] First, CDC reduced the number of days served in combat companies for selection in the study from 9 months to 6 months. The Agency also broadened the time period for study subjects from veterans who served only in the time period, 1967–1968, when the herbicide spraying was heaviest, by adding an additional six months.[34]

The Director of the CDC Center for Environmental Health and Injury Control testified that the reduction in number of days served eliminated veterans who had greater opportunities for exposure to Agent Orange. The following exchange occurred between the Subcommittee Chairman and the Director.

> Mr. WEISS. If you reduced that 9-month number, you would be eliminating the veterans with the greatest opportunity for exposure, would you not?
>
> Dr. HOUK. If we reduced the number, right.
>
> Mr. WEISS. The 9-month number.
>
> Dr. HOUK. If we had made it 6 months?
>
> Mr. WEISS. Yes.
>
> Dr. HOUK. We would have less likelihood of exposure.
>
> Mr. WEISS. That's right.
>
> Dr. HOUK. Right.[35]

In addition to its complaints about the Defense Department's troop movement records, CDC also questioned data it had received regarding the dispersion of the Agent Orange after being sprayed. The December 8, 1985, interim report discussed test missions flown over a sampling grid in 1970,

[31] Ibid., p. 1.
[32] Ibid., p. 2
[33] "Exposure Assessment for tha Agent Orange Study, Interim Report Number 2, Supplemental Information." Agent Orange Projects, Division of Chronic Disease Control, Center for Environmental Health, Centers for Disease Control, December 8, 1985.
[34] Ibid., p. 6.
[35] Hearing, 1989. Testimony of Vernon N Houk, M.D., Director, Center for Environmental Health and Injury Control, Centers for Disease Control, p. 47.

> . . . While many conditions such as the spray system, altitude, and aircraft were similar to those which prevailed in Vietnam for the Ranch Hand missions, other conditions (e.g. the number of aircraft used and vegetative cover) were different, so that results can only be used as rough estimates of herbicide dispersion. In a crosswind, the concentration decreased . . .
>
> . . . unfortunately estimates of dose would depend on knowledge of bioavailability, absorption rates, clothing worn, as well as behavioral factors such as amount of time spent in contact with vegetation, soil, and grasses, and consumption of local food and water. Data are insufficient to estimate dose.[36]

At the time CDC was diluting the study, using the rationale that the Defense Department's records were inaccurate or missing, a team of expert scientists from the National Academy of Sciences' Institute of Medicine (IOM) made a site visit to the Department's Environmental Support Group (ESG). The scientific team found the ESG records important and useable, and was critical of CDC's performance. The IOM final report stated that they were "satisfied that the ESG is capable of determining locations and fillings gaps using a contextual approach, and notes that the ESG exhibits a high degree of competence in recording data gathered from these activities." [37] The IOM also said it was "satisfied with the ESG's documented Standard Operating Procedure to fill in gaps, and was also satisfied with the methods used by teams or pairs to resolve questions which arose during contextual analysis . . . satisfied with the ESG's quality control program." [38]

ESG personnel informed the IOM team that ESG's "ability to make determinations on company locations has been hampered by CDC-imposed constraints. The ESG also pointed out that there is a considerable loss of numbers of veterans with potential exposure from the study because of CDC's stringent eligibility requirements." [39] ESG identified numerous cases of veterans who had received 10 or more exposures to Agent Orange, but had been excluded from the CDC study. For example, ESG pointed out, because CDC has eliminated all headquarters personnel from the study, if a veteran "had 170 days of combat and . . . then moved into a headquarters unit they were not included in the study . . ." [40]

After reviewing the work of ESG, the IOM team concluded that CDC had wrongly restricted the study. For example, the team stated that it was:

> concerned about the use of discrete categories to define exposure (e.g., exposure vs. non-exposure), and instead favors measuring exposure as a continuous variable . . . whenever possible. The use of discrete categories in data collec-

[36] Op cit., p 17 See footnote 33.
[37] "Site Visit to the U.S Army Environmental Support Group." Advisory Committee on the CDC Study of the Health of Vietnam veterans, National Academy of Sciences, Institute of Medicine, March 7, 1986, p 6.
[38] Ibid., pp 6–7
[39] Ibid., p 4
[40] Ibid., p 5

tion stages essentially discards valuable information, and such data can be stratified for subsequent analyses.[41]

The IOM team also said it "was perplexed about criteria established by CDC to select subjects, especially the 180 day cutoff for combat time and the exclusion of headquarters-based individuals exposed to perimeter sprays."[42] The team also found, "the criteria used to define exposure and to define who will be included in the study seem arbitrary and confusing" and concurred with ESG "that there appear to be many exposed individuals who will be excluded from the study as it is now designed."[43]

The IOM experts were also concerned that a scientific panel of the White House Agent Orange Working Group (AOWG) "is currently trying to define 'exposure' " and noted "the thinness of expertise in certain areas" of the individuals serving on the panel.[44] In conclusion, the scientific team reported that "there appear to be different kinds of exposure, and that individuals were exposed under a variety of conditions; these issues need to be addressed more carefully. The [IOM] subcommittee finds the current definition of exposure to be inadequate."[45]

The IOM findings were not reported to the White House. Therefore, the White House AOWG was misinformed when its Science Panel held a meeting three months after the IOM site visit to ESG, and reported:

> Pertinent military records have been used appropriately to locate all known herbicide spraying operations and military units and to identify individuals who may have had opportunities for exposure to Agent Orange. Limitations on the assessment of exposure opportunities are due to limitations in the records themselves.
>
> • • • • •
>
> There is unanimous agreement that an epidemiological study of ground troops' possible exposures to Agent Orange disseminated by Operation Ranch Hand fixed-wing aerial spraying, based solely on military records, does not appear to be scientifically feasible.[46]

In reaching this decision, the AOWG Science Panel noted that it "did not bring in independent evidence or experts." In light of the evidence compiled since the cancellation of the study, the committee finds that the White House's final decision was based on incomplete and erroneous information, and that pertinent information was purposefully withheld by CDC. The committee further concludes that the dilution of the study was unnecessary, was based on arbitrary criteria established by a panel controlled by the White House, and directly led to the study's collapse. The Agency Orange Exposure study failed as a result of its own design.

[41] Ibid., p 7.
[42] Ibid.
[43] Ibid., pp 11-12.
[44] Ibid., p. 13.
[45] Ibid., pp 12-13.
[46] "Minutes of the Meeting on June 17, 1986," Science Panel of the White House Agent Orange Working Group.

C. THE BLOOD SERUM ANALYSIS, WHICH WAS USED AS PROOF BY CDC THAT AN AGENT ORANGE EXPOSURE STUDY COULD NOT BE CONDUCTED, WAS BASED ON ERRONEOUS ASSUMPTIONS AND A FLAWED ANALYSIS

Using its criticism of the ESG records as its excuse, CDC and the AOWG were inclined against proceeding with the study. However, before a decision to cancel or go forward could be reached, CDC needed to test the exposure definition it had developed. The method it considered to validate the definition involved testing Vietnam veterans for traces of dioxin. At first, this was not considered feasible. Although the measurement of dioxin in humans had been achieved through the use of gas chromatography/mass spectrometry to identify the contaminant in fatty adipose tissue, Federal scientists believed there were two obstacles to using this process in the Agent Orange study. First, there was the difficulty of obtaining adipose tissue, which required surgical extraction, a procedure considered too invasive and unwieldy for a study of this sort. Second, the half-life of dioxin in animal studies proved to be less than a year, which, if extrapolated to humans, would mean the dioxin had been eliminated from the bodies of Vietnam veterans long before 1986.[47]

During a meeting of the AOWG Science Panel on June 17, 1986, representatives of CDC proposed using dioxin levels in blood serum as a surrogate for Agent Orange exposure. The minutes of the meeting indicate that the Science Panel was divided on the proposal; some thought it should be done, while others did not think it was feasible. The panel concluded:

> There is no agreement at this time whether a feasible and accurate method for validation of individual exposure status can be devised, and the science panel cannot recommend attempting a verification study.
>
> • • • • •
>
> There is unanimous agreement that if a well-designed exposure verification study fails to validate individuals' exposures as determined from military records, the Agent Orange Epidemiological Study should be discontinued.[48]

CDC overcame the difficulties of obtaining adipose tissue by developing, for the first time, a method of identifying dioxin traces in human blood. This left the second obstacle, the short half-life of dioxin, as the sole impediment. This was also overcome, according to CDC:

> The second problem of expected short half-life was changing as studies on human 2,3,7,8-TCDD exposure yielded results more compatible with a half-life much longer than 1 year. Results from a few persons in Missouri

[47] "Estimates of the Half-Life of 2,3,7,8-Tetrachlorodibenzo-p-Dioxin in Vietnam veterans of Operation Ranch Hand," James L. Pirkle, Donald G. Patterson, Donald L. Phillips, and Larry L. Needham, Centers for Disease Control, and William H. Wolfe, Joel E. Michalek, Judson C. Miner, and Michael R. Peterson, U.S. Air Force School of Aerospace Medicine, Journal of Toxicology and Environmental Health, Vol. 26, 1989, p. 166.
[48] Op. cit., p. 2. See footnote 46.

> . . . and an occupationally exposed worker in Germany . . . suggested, on the basis of last known exposure determined by history, that 5–8 years was a more reasonable estimate of 2,3,7,8-TCDD half-life for humans. In another study . . . an individual who ingested radiolabeled 2,3,7,8-TCDD and tracked his urinary and fecal excretion of the radiolabel estimated the half-life at 5–8 years.[49]

The exposure examples cited by CDC to justify a new half-life of dioxin involved situations totally unlike Agent Orange spraying in Vietnam. Yet, based on this new evidence, CDC, in collaboration with the U.S. Air Force, tested the blood of Ranch Hand veterans, as well as veterans whom CDC had selected in its exposure study. Using a half-life estimate for dioxin of 7.1 years, the blood of 646 Vietnam veterans was tested. According to CDC, only 4 percent of the non-Ranch Hand subjects had elevated levels of dioxin in their blood, and there was no correlation between exposure and dioxin in the blood.[50] CDC reached no conclusions about exposure on the basis of the study and, without further evaluation, found there was no other method to assess exposure. The final report on the blood testing found:

> The findings of this study and the conclusions from the AOWG Science Sub-Panel report on exposure assessment . . . do not identify any method for utilizing military records or self-reported exposure to distinguish between exposed and nonexposed Vietnam veterans, as would be needed for a cohort study of possible health effects.[51]

CDC's conclusion that the half-life of dioxin in the human body is 7.1 years was reached in disregard of warnings from CDC's own scientists and the peer review committee at IOM that there was not sufficient evidence to support the longer half-life. IOM informed CDC that, because of the incorrect assumptions about the half-life of dioxin, the conclusions of the blood study were not supportable. IOM informed CDC of its concerns:

> [The IOM site team has] substantial reservations about the conclusions and recommendations presented in the CDC pilot study report. The committee believes that the *conclusions* as they are now stated are not fully supported by the evidence provided in this report.
>
> Moreover, the committee urges that the *recommendations* as currently stated in the CDC pilot study report be deleted; they appear to reach well beyond the data presented and to incorporate information that goes beyond the scope of the current investigation.[52]

The IOM report criticized CDC's assumption about the half-life of dioxin. The IOM was concerned that the study was based on blood drawn 20 years after exposure to Agent Orange. The report advised

[48] Op. cit., pp. 166–167. See footnote 47.
[49] Op. cit., p. 43. See footnote 3
[50] Ibid
[51] "Review of Comparison of Serum Levels of 2,3,7,8-TCDD with Indirect Estimates of Agent Orange Exposure in Vietnam veterans," Fifth Letter Report, Advisory Committee on the CDC Study of the Health of Vietnam veterans, Institute of Medicine, June 26, 1987, pp 17–18.

that "There are several possible conditions that could have occurred between 1967 and 1987 that might result in the TCDD levels observed today." [53] The report stated that the veterans studied could have had different ranges of exposure, which due to decay of dioxin in the body, could result in the same background levels of dioxin 20 years later, or that they could have been equally exposed, but dioxin decayed in their bodies at different rates, due to physical and environmental variables.[54]

The IOM committee was particularly critical of the conclusion by CDC and the White House that the blood tests proved a complete exposure study was impossible.

> The conclusion that a full-scale cohort study is not feasible goes well beyond the scope of this study, which was conducted to assess the validity of indirect indices of exposure. If such an expansive statement is offered, it certainly warrants argumentation and documentation. The committee did not find support for this conclusion in the pilot study . . .[55]

The IOM panel was also concerned that blood was not available for a significant portion of the cohort studies: 52 percent of the veterans who did not serve in Vietnam and only 68 percent of the veterans who did serve in Vietnam.[56] The IOM team asked CDC to provide alternative explanations for the lack of correspondence between the indirect measures and current dioxin levels, and in regard to fears about Agent Orange, concluded:

> . . . it is not clear that the findings presented in this pilot study warrant complete abatement of concern. Little can be said with certainty about the TCDD levels in men 20 years ago. Moreover, background levels detected some years later do not provide assurance that no health effects will ultimately surface. Given the insufficiency of data relating the level of exposure to health outcome in humans, delayed effects of low or high doses could become apparent years after exposure occurred.[57]

IOM's comments, which were largely disregarded in the final blood serum assay report, served to remind CDC that the purpose of the blood tests was to validate the exposure definitions and scores developed by the agency and the AOWG, not to actually assess exposure. It should have come as no surprise to CDC that there was no correlation between the blood tests and exposure scores, because the scores were based on a diluted protocol that eliminated from the study the veterans who would have been the likeliest to be exposed. The Director of the CDC Agent Orange Project was aware of this problem, and warned the Director of CDC on March 17, 1986:

> If only weak correlations are found between residual TCDD levels and the exposure opportunity scores (e.g.,

[53] Ibid, p 11.
[54] Ibid
[55] Ibid, p 19
[56] Ibid, p 15
[57] Ibid, pp 19–20

there is no difference between the "high" and "low" exposure opportunity scores), it will be unknown if the failure to find a difference was due to limited Agent Orange exposure in Vietnam or to misclassificatinn of the scores.[58]

The same memorandum also stated that, while the blood serum assay was a legitimate tool for validating CDC exposure methodology, "it should be noted that current TCDD levels could bear an imperfect correlation with exposure to Agent Orange because of individual variability in both the metabolic half-life of dioxins and in post-service exposure to dioxin containing compounds." [59]

More than a year earlier, in January 1986, the senior statistician on the Agent Orange Project expressed serious reservations about using dioxin measurements to validate exposure. The statistician warned that a TCDD analysis had a substantial likelihood that there will be essentially no correlations:

> . . . there is a great danger of very poer correlation in adipose measurements separated by a long period of time. Thus, there is a substantial chance that we will find at best a very weak relation between exposure score and the adipose measurement . . . we are asking for trouble if we do TCDD measurements.[60]

The Director of the Center for Environmental Health and Injury Control stated that the senior statistician did not know what he was talking about. Dr. Houk testified, "I think he has been proven to be wrong and I discussed with him that it would be inappropriate for a senior laboratory scientist to comment on the inadequncies of a very elegant statistical design and analysis." [61] Dr. Houk's criticism is curious, given that he had selected this same statistician to direct the analysis of the study's results.[62]

The evidence is compelling that CDC was aware that the blood test study could not be the final word on the Agent Orange study. In 1987, the scientists working on the blood serum study cautioned in a provisional report:

> The study reported here measured TCDD levels as a *marker* of prior exposure to Agent Orange. It was *not* designed to detect "biologically meaningful" differences in serum TCDD levels because:
>
> 1. Levels of TCDD in man at which adverse health effects become manifest are not knewn;
> 2. Even if toxic levels of TCDD were known, the tissue half-life of TCDD in man is not precisely known, so that it would be difficult to extrapolate current

[58] "Evaluation of residual dioxin levels in Vietnam veterans as a validation of Agent Orange exposure opportunity scores," Memorandum from Peter M. Layde, M.D., M.Sc., Acting Director, Agent Orange Projects, to James O. Mason, M.D., Dr.P.H., Director, Centers for Disease Control, March 17, 1986, p. 3

[59] Ibid.

[60] "Trip Report on Meeting with Tavia Gordon, Max Halperin, and Shelby Stanton," Memorandum from John M. Karon, Senior Statistician, Agent Orange Project, to Dan McGee, Director, Agent Orange Project, January 9, 1986, p. 6

[61] Hearing, 1989, p. 67

[62] Ibid., p. 68

levels in veterans back 20 years to when exposure may have occurred; and

3. The component of Agent Orange that may have been responsible for adverse health effects is not known. Although attention has focused on the TCDD contaminant, the two active Agent Orange ingredients, 2,4-D and 2,4,5-T, also may cause adverse health effects. . . . Different components of Agent Orange may have been responsible for different manifestations.[63]

One of the scientists on the Agent Orange Project testified that CDC, despite its public claims to the contrary, "had no idea about its [dioxin's] half-life. We had some conjectures about the half-life of dioxin but we didn't have anything certain." [64] He added:

> Also, we weren't certain about the dosage that would produce an effect. No one knew the relative importance of the various routes of exposure. We didn't know much at all about the distribution of dioxin within the body. There's an assumption that it stores itself in fat tissue 11 times more frequently than in serum but this sort of information, I think, is very questionable.[65]

CDC had already diluted the study protocol to the point it would not identify the veterans most likely to have been exposed, to avoid a lengthy document review. The decisions to dilute were made for reasons of expediency. With its manipulation of the half-life of diexin, CDC seemed to be trying to justify an intentionally flawed exposure assessment methodology with tha blood serum analysis. The blood assay test was more a method of convenience than an exhaustive scientific approach. As Dr. Smith testified:

> We damned the historical records with overemphasis on minor problems with ESG. We ignored ether sources of records and relied too much on unreliable, anecdetal reports. We played with the half-life of dioxin using only those studies and reports that would advance the concepts of what the model which we wanted to use would say at the time. . . .
>
> We ignored most of the medical literature on dioxin. We had some excellent references but we only focused on a few papers, especially when the adipose tissue proposol came along. The focus was only on a few papers that supported what we had in mind, or, what we had ultimately come to.[66]

Dr. Michael Kafrissen worked on the Agent Orange Projects and had been osked by CDC to evaluate the half-life of dioxin in the human body. Although he said there was semo preliminary evidence indicating a half-life of 7.1 years for dioxin in humans in

[63] "Comparison of Serum Levels of 2,3,7,8-TCDD with Indirect Estimates of Agent Orange Exposure in Vietnam veterans—Provisional Report," Agent Orange Projects, Division of Chronic Disease Control, Center for Environmental Health, Centers for Disease Control, July 1987, p. 18

[64] Hearing, 1989 Smith testimony, p. 81

[65] Ibid

[66] Ibid., p. 82

some situations, he stated, "I don't believe at this time there is sufficient information to say that this number obtains for all men at all times under all physical circumstances." [67] Dr. Kafrissen also testified that "We did not know all of the critical levels—and I don't believe we now know—of dioxin that is going to effect a problem in humans. For that reason, we were concerned with the possibility that men may have been affected, may have been exposed and that we would no longer be able to judge that based on these laboratory specimens." [68]

The assumption that dioxin had a longer half-life in the human body than previously believed was based on studies of individuals who were directly exposed to high doses of dioxin in laboratory accidents, one study of a scientist who ingested dioxin in high doses to evaluate half-life, and tests conducted of veterans who worked in Operation Rand Hand, directly spraying and handling Agent Orange in large amounts. These subjects cannot be compared to Vietnam veterans who had less direct exposure, possibly over longer periods of time. The large, short-term exposure to undiluted chemicals as the result of industrial accidents is quite different from the possible long-term exposure to Agent Orange in which the contaminants were diluted with other substances. Obviously, dioxin exposure is different in these subjects and the elimination of dioxin traces would be entirely different than in the subjects mentioned earlier. While studying the half-life of dioxin in highly exposed veterans and workers was relevant to the CDC Agent Orange Study, the committee finds the conclusion that the 7.1 years half-life in highly exposed individuals can be extrapolated to all Vietnam veterans to be unsupportable.

Even the method by which CDC determined the half-life—called first order kinetics—may not have been the correct way of assessing dioxin elimination from the human body. The scientists who conducted the half-life study cautioned:

> With just two serum 2,3,7,8-TCDD values per veteran, it is not possible to definitively state that a first-order kinetic model is appropriate to describe the decline in serum 2,3,7,8-TCDD concentrations over time or that a more complex model is needed.[69]

Based on the complete record of the CDC Agent Orange Studies, the committee believes there was a two-part course selected by the Agency that guaranteed the eventual cancellation of the study. First, CDC ignored the military records experts at the Pentagon, created its own use of the records to establish exposure, and then diluted the study to the point that numerous veterans who were most likely to have high exposure were eliminated from the study. Second, using the flawed exposure definition it had developed, CDC then attempted to justify it with the blood serum assay, which, itself, was based on false assumptions about the chemical's half-life in the human body. Unsound assumptions about the half-life of

[67] Ibid. Testimony of Michael E. Kafrissen, M.D., former epidemiologist, Centers for Disease Control, p. 107.
[68] Ibid., pp. 106-107
[69] Op. cit., p. 170. See footnote 47.

dioxin were used to validate badly-designed exposure assessments. Given these restrictions, it would have been impossible to validate exposure.

The committee also finds that, in adopting these courses of action, CDC disregarded or ignored the warnings from its own scientists, Defense Department officials, and the expert committee assembled by the IOM.

D. THE WHITE HOUSE COMPROMISED THE INDEPENDENCE OF THE CDC AND UNDERMINED THE STUDY BY CONTROLLING CRUCIAL DECISIONS AND GUIDING THE COURSE OF RESEARCH AT THE SAME TIME IT HAD SECRETLY TAKEN A LEGAL POSITION TO RESIST DEMANDS TO COMPENSATE VICTIMS OF AGENT ORANGE EXPOSURE AND INDUSTRIAL ACCIDENTS

The subcommittee's review of Executive Branch records demonstrates that two components of the White House, the Agent Orange Working Group (AOWG) and the Office of Management and Budget (OMB), monitored and controlled the CDC Agent Orange Project. Top administration officials such as Attorney General Edwin Meese and White House Chief of Staff James Baker had ultimate decisionmaking authority for approving and eventually canceling the exposure study, but the nuts and bolts of the work were handled by the AOWG and OMB.

While Agent Orange was the impetus for the establishment of the White House advisory committee under President Carter, the panel's mandate was not limited to the war-time defoliant. Its purview included the effect of herbicide contaminants in addition to Agent Orange.

The first responsibilities of the White House panel were to instruct the Air Force to conduct the study of Ranch Hand personnel and to oversee both the Ranch Hand study and the epidemiological study of Agent Orange.[70]

In June 1983, the Reagan Administration decided to revise the charter of the White House panel by eliminating its mandate to explore the effects of all herbicides and contaminants and concentrating the work of the group only on Agent Orange. In a memorandum from Robert B. Carleson, Special Assistant to the President, to White House aide Jack Svahn, it was decided:

> . . . the task of the Working Group on Agent Orange be concentrated so that its work can be completed in a timely manner. Therefore, please ensure that your working group deals only and specifically with the possible long term adverse health effects of exposure to Agent Orange and Vietnam veterans.[71]

The AOWG was the successor to the White House Advisory Committee on Special Studies Relating to the Possible Long-Term Health Effects of Phenoxy Herbicides and Contaminants. The origi-

[70] Memoranda to the Secretary of Defense and the Administrator of Veterans Affairs, from Stuart E. Eizenstat, Assistant to the President for Domestic Affairs and Policy, September 16, 1980
[71] "Task Assignment of the Working Group on Agent Orange," Memorandum from Robert B. Carleson, Special Assistant to the President, to Jack Svahn, Chairman, Working Group on Agent Orange, June 2, 1983.

nal advisory committee was established on December 11, 1979, in a memorandum drafted by Stuart E. Eizenstat, Assistant to President Jimmy Carter for Domestic Affairs and Policy. The advisory panel's mission was to assure that all Federal research into herbicides and contaminants provide reliable data, and to provide technical support to Federal agencies working on the research.[72]

The original mandate to focus the White House panel on the effects of all herbicides was abruptly altered by the Reagon White House. By focusing the work of AOWG on Agent Orange only, the administration laid the groundwork for manipulating the study to the point of uselessness.

A possible reason that the White House chose this path is revealed in confidential documents prepared by attorneys in OMB. The White House was deeply concerned that the Federal Government would be placed in the position of paying compensation to veterans suffering diseases related to Agent Orange and, moreover, feared that providing help to Vietnam veterans would set the precedent of having the United States compensate civilian victims of toxic contaminant exposure, too.

These concerns were included in a series of memoranda prepared by an OMB attorney about pending legislative proposals to compensate victims exposed to Agent Orange and nuclear radiation. These proposals, OMB warned, "have enormous fiscal implications, *potentially in the hundreds of billions of dollars.*"[73] In discussing H.R. 1961, a bill pending in the House of Representatives that would provide compensation to veterans exposed to Agent Orange and nuclear radiation, OMB called the legislation "our first key challenge on toxic compensation—and it has significant ramifications for other, more costly compensation proposals. It is therefore extremely important that we organize our position and response . . . [74]

The ramifications feared by the White House were delineated in a second memorandum. A major worry was that the legislation, if passed, would make it hard for the White House to prevent compensation to victims of other types of contaminants:

> The bill will make it far more difficult to stop broader victims compensation schemes involving hazardous wastes and substances. Dioxin—the toxic ingredient in Agent Orange—is a major issue in this area (Love Canal and Times Beach are largely dioxin exposure cases); *we will be in the tenuous position of denying dioxin exposure compensation to private citizens while providing benefits to veterans for in many instances lower levels of exposure.*[75]

The White House also feared that passage of the legislation would damage its efforts to prevent compensation for claims involving nuclear radiation. "The radiation portion of the bill will undermine the United States' position in pending radiation litigation. The *Allens* case, involving $2 billion in claims, is still under advisement before a Utah federal judge." [76]

A subsequent memorandum reiterated these concerns and expanded upon them. In regard to nuclear radiation, OMB warned:

> Many residents near the test sites received cumulative exposures far in excess of the single doses to which veterans were exposed. These residents will undoubtedly demand compensation for these far greater levels of cumulative exposure. . . . There is understandable concern at Justice that H.R. 1961 will effect the outcome of that case.
>
> The bill will certainly be used by anti-nuclear extremists as providing credibility for their alarmist claims on the dangers to the public from nuclear weapons facilities, nuclear reactors, transportation of nuclear materials, underground testing, etc. This may have serious national security ramifications.[77]

So strident was the administration in its belief that the Federal Government should not be liable for exposure to toxic chemicals that the Justice Department ordered the Defense Department not to assist the Special Master overseeing the legal settlement between the manufacturers of Agent Orange and Vietnam veterans. On May 22, 1986, the Director of the Defense Department's ESG asked the Justice Department if he could assist the Special Master in the evaluation of herbicide spray and troop movement records already provided to the Special Master. The assistance, the director wrote, would "prevent duplication, delay, misinterpretation and costs against the funds set-aside for Veterans' awards." [78]

The Justice Department ordered the Defense Department not to cooperate with the Special Master, advising that "government employees not be made available to render advice and assistance concerning the allocation of settlement fund proceeds." [79]

A month later, the Director of ESG was asked to testify before a subcommittee of the House Committee on Veterans Affairs about the results of the work of the Agent Orange Working Group. In a memorandum to the Defense Department Adjutant General, the Director reported that much of his testimony was "deleted by OMB. . . . Such results are neither forthright or responsive. . . . the testimony has been rewritten and its guts torn out. . . ." [80]

In light of these confidential actions by the Justice Department and OMB, and given the White House's legal concerns that the Federal Government could be liable in toxic contaminant law suits, it is apparent why the charter of the AOWG was revised and limit-

[72] Charter, Advisory Committee on Special Studies Relating to the Possible Long-Term Health Effects of Phenoxy Herbicides and Contaminants," as amended May 1984

[73] "Compensation for Low-Level Radiation Exposure and Related Developments," Executive Office of the President, Office of Management and Budget, Memorandum to Ed Meese, Joe Wright, Jay Keyworth, Fred Fielding, and M B. Oglesby, from Mike Horowitz, December 6, 1983, p 1

[74] Ibid , p. 3.

[75] "Agent Orange/Radiation Compensation Legislation," Executive Office of the President, Office of Management and Budget, Memorandum to Dave Stockman, Joe Wright, Jay Keyworth, and Fred Fielding, from Mike Horowitz, January 17, 1984, p 2

[76] Ibid

[77] "H.R. 1961, Agent Orange and Atomic Veterans Relief Act," Executive Office of the President, Office of Management and Budget, Memorandum to Ed Meese, Jack Svehn, Joy Keyworth, and B Oglesby, from Mike Horowitz, February 6, 1984, p. 2.

[78] Letter from Robert C. Longstreth, Trial Attorney, Torts Branch, Civil Division, Department of Justice, to Richard S Christian, Director, U.S. Army and Joint Services Environmental Support Group, June 3, 1986. (Letter cites Christian letter of May 22, 1986.)

[79] Ibid.

[80] Memorandum from Director, Environmental Support Group, to The Adjutant General, July 30, 1986

ed to Agent Orange only. At the time of the revision, numerous Federal research projects were being conducted of domestic and civilian worker exposure to herbicides.[81] By revising the charter to ignore the dozens of Federal studies dealing with herbicides other than Agent Orange, the White House forced the AOWG to overlook a wide range of issues, not only related to Agent Orange, but vital to the health of civilian workers, as well. Thus, the White House would not have to deal with potential liabilities involving herbicides other than Agent Orange.

The committee believes that, given the White House's predisposition against compensating victims of toxic contamination, White House officials should have recused themselves from involvement in the deliberations about the CDC Agent Orange Studies and that the AOWG should not have been given the authority to approve or

[81] The following studies were reported to the Agent Orange Working Group in a document, "Federally Sponsored Human Studies Related to Agent Orange," April 11, 1983, National Institute of Occupational Safety and Health (NIOSH), Investigation of Leukemia Cluster in Madison County, Kentucky, Allegedly Associated with Pentachlorophenol Treated Ammunition Boxes, Centers for Disease Control (CDC), Birth Defects and Military Service in Vietnam Study; NIOSH Dioxin Registry, National Institute of Environmental Health and Safety (NIEHS), Establishment and Maintenance of an International Registry of Persons Exposed to Phenoxy Acid Herbicides and Contaminants; NIOSH Soft Tissue Sarcoma Investigation, National Cancer Institute (NCI), Case Control Study of Lymphoma and Soft Tissue Sarcoma; NCI Study of Mortality Among Pesticide Applicators from Florida; CDC Epidemiologic Study of Ground Troops Exposed to Agent Orange during the Vietnam Conflict; Veterans Administration (VA), Vietnam veterans Mortality Studies, Vietnam veteran Identical Twin Studies, Survey of Patient Treatment File for Vietnam veteran In-Patient Care, Agent Orange Registry Examinations, TCDD in Body Fat of Vietnam veterans and Other Men, Retrospective Study of Dioxins and Furans in Adipose Tissue of Vietnam Era Veterans; Department of Defense (DOD), Epidemiologic Investigation of Health Effects in Air Force Personnel Following Exposure to Herbicide Orange, Armed Forces Institute of Pathology Agent Orange Registry of Vietnam veteran Biopsy Tissues; Environmental Protection Agency (EPA), Report of Assessment of a Field Investigation of Six-Year Spontaneous Abortion Rates in Three Oregon Areas of Relation to Forest 2,4,5-T Spray Practices, National Pesticide Monitoring Project of Human Adipose Tissue; Department of Agriculture (DOA), A Case Control Study of the Relationship Between Exposure to 2,4-D and Spontaneous Abortions in Humans, Exposure Measurements of Mixers, Loaders and Applicators of 2,4-D on Wheat, Exposure of Forest Workers to Ground Applications of 2,4-D, Department of Health and Human Services (HHS), Bioassay of Octochlorodibenzo-p-dioxin, Carcinogenesis Bioassay of 2,3,7,8-Tetrachlorodibenzo-p-dioxin in Swiss Webster Mice, Carcinogenesis Bioassay of 2,3,7,8-Tetrachlorodibenzo-p-dioxin in Osborn-Mendel Rats and B6C3F1 Mice, Bioassay of a Mixture of 1,2,3,6,7,8- and a Mixture of 1,2,3,6,7,8-Hexachloro-dibenzo-p-dioxins for Possible Carcinogenicity, Comparative Species Evaluation of Chemical Disposition and Metabolism of 2,3,7,8-Tetrachlorodibenzofuran in Rat, Monkey, Guinea Pig and Two Stroine of Mice, Neurotoxicity of 2,4,-D in Rodents, Studies of the Chemical Disposition and Metabolism of Octochlorodibenzodioxin, Effects of Agent Orange Components on Male Fertility and Reproduction, Mutagenicity Studies of TCDD, Implications of Low Level Exposure of Dioxins, Mechanisms of Toxicity of the Chlorinated p-dioxins, Research Toward Understanding the Molecular Level Mechanisms of Toxicity of TCDD and Related Compounds; Synthesis of Selected Tetrachlorodibenzo-p-dioxins and Related Compounds as Analytical Standards, Matrix Effect and Sub Parts-per-billion Quantitative Analysis of TCDD by Mass Spectrometry—With Special Reference to Milk, Toxic Actions of Dioxins, Xenobiotic Induction of Pleiotropic Responses in Liver, Molecular, Biochemical Actions of Chlorinated-p-dioxins, Mechanisms for Toxicity of Chlorinated Dibenzo-dioxins, Modular basis of Dioxin toxicity in Keratinocytes; EPA, Evaluation of Large Scale Combustion Sources, Evaluation of Municipal Waste Combusters, Bacterial Decomposition of TCDD, Investigation of Bioavailability to Fresh Water Fish of TCDD's in Fly Ash, Analysis of Environmental Samples for PCDD's and PCDF's, DOA, Survey of Phenoxy Herbicide Use by Agricultural Commodity, Survey of Phenoxy Herbicide Literature, Photolysis of 2,4,5-T, Biological and Economic Assessment of 2,4,5-T and Silvex, TCDD Residue Monitoring in Deer; DOD, Environmental Chemistry of Herbicide Orange and TCDD; VA, Review of Literature on Herbicides, Including Phenoxy Herbicides and Associated Dioxins, Urinary 6-Hydroxy Cortisol, Physiological and Pharmacologic Studies, Effect of TCDD on Lipid Metabolism, Mechanisms of Dioxin Inducted Toxicity Using the Chloracne Model, Behavioral Toxicity of An Agent Orange Component of 2,4-D, Effects of 2,3,7,8-Tetra-chlorodibenzodioxin on Hepatobiliary Function in Animals, Mechanism of TCDD Absorption and Toxicity on Lipid and Lipoprotein Metabolism, Metabolism of the Herbicides Present in Agent Orange and Agent White, TCDD Exposed Rhesus Monkeys Effects on Behavior and Stress Hormones, Neuromuscular Toxicity of Agent Orange, Effects of Low Dose TCDD on Mammalian Chromosomes and Liver Cells, Mechanism of Porphyria Caused by TCDD and Related Chemicals, Effects of Agent Orange on Sleep.

disapprova CDC's activities. The potential to wrongly influence the outcome of the CDC studies inherent in this conflict of interest was realized when White House officials directly interceded in the decision that steered the study in the wrong direction, and ultimately resulted in its failure.

A July 18, 1986, OMB memorandum provides evidence that it was the White House, not CDC, that was making decisions during possibly the most crucial phase of the Agent Orange exposure study. It was a time when the military records were considered unsuitable for use in the study, and the entire project was in danger of being canceled. The cancellation was averted when CDC proposed testing the blood of Vietnam veterans for dioxin traces. The memorandum presents information about the White House AOWG's "decision to proceed with the development of a protocol for testing the dioxin levels in blood for Vietnam ground troop veterans."[82] The memorandum states that the decision on whether to cancel the study will be influenced by CDC's public testimony before the House Veterans Affairs Committee on July 31, 1986. According to the memorandum, "It is important that the hearing *testimony leave the AOWG with options* on the future of the Agent Orange study. In particular, the testimony should point out that the blood test may only have a very limited usefulness in studying individuals with low levels of dioxin exposure."[83]

The memorandum contains an admission that the final decision was based on the Federal Government's legal culpability, not necessarily the independent work of scientists.

> The decision should take into account the legal implications of the blood test (the risks associated with testing individuals and the potential that claims against the government would be made by individuals who have higher than "normal" dioxin levels in their blood). I have discussed these issues briefly with Justice attorneys who would be available to evaluate the pilot study proposal for the legal risks. Any evaluation should be done prior to the next AOWG meeting so that the information may be used in the decision on the pilot study.[84]

So fearful was the White House that it might have to compensate Americans exposed to contaminants, it pressured CDC to refute the blood serum test as a measure of exposure to Agent Orange, even before it commenced. To avert possible future claims for compensation from veterans, the memorandum states, *"It is important that testimony and other public comments not associate the measurement of dioxin in blood with causation."*[85] The memorandum recommended that the White House contact the Director of CDC and encourage him to "be explicit that developing a measure of dioxin content in blood is neither a link to cause of exposure nor proof of a cause and effect relationship between dioxin and disease."[86]

[82] "Agent Orange Study," Executive Office of the President, Office of Management and Budget, to Debbie Steelman from Sarah Ducich, July 18, 1986, p 1
[83] Ibid., p 2.
[84] Ibid
[85] Ibid
[86] Ibid

The memorandum also represents evidence that the CDC study was doomed to failure by the White House, long before its final cancellation. Why else would the conclusions be reached that the blood dioxin measurement cannot be linked to Agent Orange, even before the test began? Perhaps most instructive of the White House's attitude is that it was its panel, the AOWG, that canceled the Agent Orange study, not CDC.

When the blood test, which the White House had allowed but classified as inconclusive even before it began, was finally completed in 1987, apparently showing no higher levels of dioxin in the blood of Vietnam veterans, the AOWG moved quickly. On August 27, 1987, the Chairman of the AOWG informed the Chairman of the White House Domestic Policy Council, "it has been concluded that military records cannot support a valid epidemiological study of the health effects of Agent Orange exposure on Vietnam veterans . . . I advise you to recommend to the Domestic Policy Council that the Agent Orange exposure study be cancelled." [87]

Two months later, the Director of CDC acknowledged the instructions to cancel the study. ". . . AOWG has instructed CDC to begin the process of cancelling the contracts and closing out all activities related to the Agent Orange Exposure Study." [88]

The AOWG had been riding herd over CDC from the beginning of the study. The AOWG had ordered that all Federal research be submitted to the White House panel prior to public release. On September 20, 1984, the panel ordered that ". . . all documents relating to Agent Orange research studies slated for review by any person or organization outside the Federal Government be submitted first to the Chair, AOWG." [89] After the study was canceled, the White House maintained its insistence on controlling any Federal scientific efforts related to Agent Orange. On April 1, 1988, the Chairman of the AOWG sent a memorandum to members of the panel, advising them that the future release of any information related to Agent Orange must be cleared by the AOWG.

> The release of any report, without the review mandated by the Agent Orange Working Group procedures, could constitute a serious breach and may undercut our credibility. Any premature release could cause embarrassment to the government.
>
> Research findings and conclusions must be submitted to the AOWG 48 hours prior to release for review, comment and clearance before going to Congress or the public.[90]

[87] Letter from Don M. Newman, Chair Pro Tempore, Domestic Policy Council Agent Orange Working Group, to Edwin Meese, Chair Pro Tem, Domestic Policy Council, The White House, August 27, 1987.

[88] Hearing, 1989, pp. 65-66. Note to Don Newman, Chair, Domestic Policy Council Agent Orange Working Group, from James O. Mason, M.D., Director, Centers for Disease Control, October 28, 1987.

[89] "Accomplishing the AOWG Mission," Memorandum From Edward N. Brandt, M.D., Chair, Pro Tempore, to Members, Cabinet Council Agent Orange Working Group, September 20, 1984.

[90] "Clearance of all studies and press releases by the Domestic Policy Council Agent Orange Working Group," from Don M. Newman, Chairman, Domestic Policy Council Agent Orange Working Group, to Members, Domestic Policy Council, Agent Orange Working Group (DPC/AOWG), April 1, 1988.

E. THE FEDERAL GOVERNMENT HAS SUPPRESSED OR MINIMIZED FINDINGS OF ILL HEALTH EFFECTS AMONG VIETNAM VETERANS THAT COULD BE LINKED TO AGENT ORANGE EXPOSURE

The Agent Orange Exposure Study was one of three parallel projects assigned to CDC involving the health of Vietnam veterans. The other two were the Vietnam Experience Study (VES), to determine the health status of veterans of Vietnam, and the Selected Cancers Study, conducted to determine if Vietnam veterans had been susceptible to a group of rare cancers. The key to the White House's legal strategy of not paying compensation for any type of toxic contamination was the cancellation of the exposure study. Once the exposure phase of the studies was canceled, on the premise that assessing exposure was scientifically impossible, Federal scientists were able to dismiss any link between diseases and maladies they discovered and Agent Orange.

Two examples involve the CDC's findings regarding birth defects involving the offspring of Vietnam veterans and the semen analysis conducted of the Veterans in the VES. CDC found that Vietnam veterans were more likely than non-Vietnam veterans to report birth defects. The study also concluded that Vietnam veterans reporting exposure to herbicides are at even greater risk of reporting miscarriages, birth defects, serious health problems, and infant mortality.[91]

Any possible link between herbicide exposure and the reported birth defects was dismissed by CDC because of the cancellation of the exposure study.

> The findings from a recent study in which current dioxin . . . body burdens in Vietnam and non-Vietnam veterans were assessed suggest that self-reported herbicide exposure may not be a valid estimate of actual herbicide exposure. Among Vietnam veterans, there was no evidence of elevated serum dioxin levels, and no correlation between average dioxin levels and self-reported exposure to herbicides in Vietnam. Thus, the herbicide exposure index used here may reflect the level of concern and anxiety Vietnam veterans have about the impact of Agent Orange on their health and health of their children.[92]

CDC's review of birth records found that the offspring of Vietnam veterans were twice as likely to have digestive system birth defects and were also twice as likely to suffer early neonatal death.[93] The birth records' review also indicated that the offspring of Vietnam veterans were more susceptible to cerebrospinal malformations, such as spina bifida, anencephaly, and hydrocephalus. CDC explained this problem as an underreporting of the birth defects among non-Vietnam veterans, rather than an excess among Vietnam veterans.[94] CDC's semen analysis of Vietnam veterans also found problems:

[91] "Health Status of Vietnam veterans, Volume V, Reproductive Outcomes and Child Health," Vietnam Experience Study, Centers for Disease Control, January 1989, pp. 21-29.

[92] Ibid., pp. 41-42.

[93] Ibid., pp. 72-73.

[94] Ibid., pp. 84-85.

> Mean sperm concentration was 20% lower for Vietnam veterans than for non-Vietnam veterans.
>
> * * * * *
>
> Specimens from Vietnam veterans had a lower mean proportion of morphologically "normal" sperm than did speciments from non-Vietnam veterans . . . specimens from Vietnam veterans were more likely to contain larger and more tapered sperm. . . . Both the mean cell perimeter and the mean length of the major axis of the sperm cells were significantly larger for Vietnam than for non-Vietnam veterans.[95]

Although CDC could not explain definitively why Vietnam veterans had low sperm counts and altered sperm shapes, it quickly concluded there was no link to Agent Orange:

> The possibility that exposure to dioxin-containing herbicides may have affected the sperm of Vietnam veterans is a potential concern. However, this explanation seems unlikely, since in a recent study we found that few Army ground troops were heavily exposed to dioxin-containing herbicides.[96]

The committee finds CDC's conclusion derived from the canceled exposure study that few ground troops were exposed to Agent Orange to be a false and misleading interpretation of its own study. The exposure study found that CDC could "not identify any method for utilizing military records or self-reported exposure to distinguish between U.S. Army ground combat troops who were and were not exposed to Agent Orange in Vietnam . . ."[97] The study did not find that few ground troops were exposed, the reason used to dismiss any relation between birth defects and low sperm counts by CDC.

"We never did an Agent Orange study. The Agent Orange exposure component was deemed not to be feasible based upon the validation study and that study of TCDD exposure was never done," admitted Dr. Vernon Houk, Director of the CDC office which conducted the study.[98]

The canceled CDC study, the study "we never did," according to Dr. Houk, had become a convenient way for the Federal Government to dismiss any link between Agent Orange and health problems among Vietnam veterans, and deny liability for claims involving the herbicide. CDC's own Vietnam Experience Study contained preliminary indications that the liability could be large. CDC's findings showed that psychological problems such as Post Traumatic Stress Disorder, depression, anxiety, and psychopathology were more prevalent among Vietnam veterans than non-Vietnam veterans. Vietnam veterans were more likely to have histories of hospitalizations, hypertension, benign growths, chloracne, ulcers, hepatitis, liver conditions, urinary tract problems, and fertility difficulties. They were more prone to abnormal clinical findings, such as possible left ventricular hypertrophy, hearing loss, peripheral neuropathy, evidence of past hepatitis B infection, and abnormal laboratory findings, such as gamma-glutamyl transferase, fasting glucose, thyroid-stimulating hormone, and occult stool blood.[99]

[95] "Health Status of Vietnam veterans, Volume III, Medical Examination," Vietnam Experience Study, Centers for Disease Control, January 1989, p. 207.
[96] Ibid., p. 220.
[97] Op. cit., p. 4. See footnote 3.
[98] Hearing, 1989. Houk testimony, p. 44.

CDC was also aware of other clinical effects that were assumed to be related to exposure to the chemical constituents of Agent Orange. Studies of workers exposed to dioxin found a host of effects.

TABLE OF CLINICAL EFFECTS ASSOCIATED WITH EXPOSURE TO THE CONSTITUENTS OF AGENT ORANGE[100]

Dermatological: Chloracne, porphyria cutanea tarda, hyperpigmentation and hirsutism, contact dermatitis.

Hepatic: Liver damage (. . . mild fibrosis, fatty changes, hemofuscin deposition, parenchymal-cell degeneration), increased serum hepatic enzyme levels.

Other internal: Disorders of fat metabolism, disorders of carbohydrate metabolism, cardiovascular disorders . . . elevated serum cholesterol levels, abdominal pains and diarrhea, pancreatic disorders.

Respiratory: . . . SMR for lung cancer, dyspnea. . . .

Genito-urinary: Hemorrhagic cystitis, hematuria proteinuria, SMR for malignant neoplasms of the genito-urinary organs and the bladder.

Neuro-muscular: Asthenia, fatigue, headaches, sleep disturbances, sweating, irritability, confusion, peripheral neural damage, polyneuropathies, delayed peripheral nerve conduction, encephalomyelitis sensorial impairments. . . . Hyperesthesia, impotence . . . lassitude and weakness, vertigo, ataxia, hyporeflexia, rigidity, myotonia, pain in the extremities, joint pain, severe aches in the lower extremities, difficulty in muscular and mental coordination, profound muscular weakness, neuroarthropathy.

Other: Loss in body weight, thymic atrophy, decreased immune competence.

At the time the Agent Orange exposure study had been canceled, CDC's reputation for objectivity and accuracy was beyond reproach. Thus, its false interpretation that few ground troops had been exposed to Agent Orange was accepted as gospel by the scientific community. Other Federal agencies, particularly the VA, were quick to parrot CDC's work and apply it to other research. For example, a 1987 report by the VA on soft tissue sarcoma and military service in Vietnam found that subgroups of ground troops studied who appeared to have higher opportunities for exposure to Agent Orange were at greater risk of contracting the rare cancer, and

[99] Ibid Testimony of Dr. Steven Stellman, pp. 178-179
[100] "Observed Clinical Effects of 'Agent Orange,'" Memorandum from Dennis Smith, Visiting Scientist, Agent Orange Projects, Centers for Disease Control, to Dan L. McGee, Ph.D., Senior Statistician, Agent Orange Projects, January 30, 1985, pp. 1-2.

that Army veterans who served combat missions showed a 2.6 times elevated risk of soft tissue sarcoma, as compared to veterans who did not serve in combat.[101]

The study concluded that "the possibility of a modestly increased risk of STS associated with Agent Orange exposure in Vietnam among select groups of Vietnam veterans can be neither confirmed nor ruled out in this study. Additional studies using better characterization of exposure are needed to answer this question." [102] The researchers had planned to conduct such a study. "Initially, an elaborate computer matching of troop location to recorded aerial spray missions . . . was planned. However, an expert government panel has subsequently determined that military records alone could not be used to locate troops with enough precision to allow a scientifically valid estimate of the likelihood of exposure to herbicides." [103] The expert Government panel to which the researchers referred is the AOWG, which based its conclusions on the CDC exposure study.

The VA also downplayed the findings of a mortality study it conducted of Army and Marine Corps veterans of Vietnam. The study found that Marines serving in Vietnam had statistically significant higher elevations of lung cancer and non-Hodgkin's lymphoma, two diseases associated with exposure to phenoxy herbicides.

> The veterans who served in the Marine Corps in Vietnam were seen to have a statistically significant . . . excess of non-Hodgkin's lymphoma when compared with Marines who did not serve in Vietnam.
>
> • • • • •
>
> Non-Hodgkin's lymphoma has been associated with exposure to phenoxy herbicides, arsenicals, dapsone, and certain viruses. The men who served in Vietnam had the potential for exposure to all of these agents. Agent Blue, a herbicide used in Vietnam, was an organic arsenical compound and dapsone, a sulfone, was used as an antimalarial drug by some of the troops in Vietnam. Dapsone has been shown to cause lymphomas in laboratory animals. Dapsone was given mainly to troops stationed in I Corps and the central highland areas of Vietnam where falciparum malaria was prevalent. Most of the Marines in Vietnam served in I Corps.[104]

Dr. Lawrence Hobson, the Director of the VA's Office of Environmental Medicine, testified that the study did not find significantly higher levels of non-Hodgkin's lymphoma and lung cancer. He contended that a "greater proportion" of the subjects studied died from those diseases.[105]

[101] "Soft Tissue Sarcoma and Military Service in Vietnam: A Case-Control Study," Han Kang, Dr PH., Frona Enziger, M.D., Patricia Breslin, Sc.D., Michael Feil, M.S., Yvonne Lee, M.S., and Barclay Shepard, M.D., JNCI, Vol. 79, No. 4, October 1987.

[102] Ibid.

[103] Ibid

[104] "Proportionate Mortality Study of US Army and US Marine Corps Veterans of the Vietnam War," Patricia Breslin, Sc.D, Hon K. Kang, DrPH; Yvonne Lee, MSc; Vicki Burt, ScM, and Barclay M. Shepard, MD, Journal of Occupational Medicine, Vol 30, No. 5, May 1988.

[105] Hearing, 1989 Testimony of Lawrence Hobson, M.D., Director, Office of Environmental Medicine, Veterans Administration, p. 138.

> It isn't fair to say that you had more deaths among the marines or a higher rate of death or a higher incidence of death from soft tissue sarcoma among those marines.
>
> The only thing you can say is that more of the ones who died seemed to have died from soft tissue sarcoma than from say heart disease or lung disease or some other form of cancer.[106]

Dr. Hobson's attempt to minimize the VA's finding that Marines were at greater risk of certain diseases obfuscates the facts uncovered by the Agency's research. The committee believes that Federal scientists have an obligation to use pertinent information regarding the health of Vietnam veterans as a tool for further exploration of the risks associated with service in Vietnam. Instead, the VA has consistently attempted to dismiss the relevance of the information to allay the concerns of Vietnam veterans.

Admiral Elmo R. Zumwalt, former Chief of Naval Operations, and more recently a special advisor to the Secretary of Veterans Affairs on Agent Orange, testified before the subcommittee of a conspiracy to withhold the truth about the herbicide from the public.

> The sad truth which emerges from my work is not only that there is credible evidence linking certain cancers and other illnesses with Agent Orange, but that government and industry officials credited with examining such linkage intentionally manipulated or withheld compelling information of the adverse health effects associated with exposure to the toxic contaminants contained in Agent Orange.[107]

Dr. Daniel Thau Teitelbaum, a toxicologist who, through litigation involving herbicide manufacturers, has reviewed their internal records, testified that the companies had withheld information about toxic contaminants in their products. He said the contaminants, called xanthen-9-ones, are toxic in animal species and are contained in 2,4-D, a chemical prevalent in herbicides, including homeowner's weed killers.[108] Dr. Teitelbaum testified that the presence of these contaminants had not been reported to the Environmental Protection Agency or State registration agencies.[109]

An epidemiologist with the National Cancer Institute, Dr. Shelia Hoar Zahm, testified that a recent study she conducted, scheduled for publication in September 1990, has proven 2,4-D to be a carcinogen in agricultural workers who use herbicides with that ingredient.[110]

2,4-D was a major ingredient of Agent Orange, but has not been explored in Federal research regarding the effects of the herbicide on Vietnam veterans.

[106] Ibid

[107] Hearing, 1990 Prepared statement of Adm Elmo R. Zumwalt, Jr., p 4

[108] Ibid

[109] Ibid

[110] Ibid

V. Recommendations

A. Congress should require the Department of Defense to create an Agent Orange exposure index

In light of the committee's determination that the CDC Agent Orange Exposure Study was flawed and canceled based on erroneous information, the committee believes that an exposure index, matching troop movement records to spray data, still needs to be and can be developed. The committee believes that the Department of Defense has the expertise and resources to conduct such an exposure index—provided adequate, independent peer review is provided by expert bodies not associated with the Department—and recommends that Congress mandate the development of an index.

B. When an adequate exposure index is developed, the Federal government should contract through the National Academy of Sciences for a private, independent epidemiological study matching the health outcomes of Vietnam veterans against the exposure index

The development of an exposure index would be only the first part of a study determining the association or non-association of illness to Agent Orange exposure. Given the bias demonstrated by Federal agencies in the past, the committee believes veterans would be better served by an epidemiological study prepared by objective scientists. Using the index developed by the Department of Defense, it is suggested that a private organization be awarded a contract, to be administered by the National Academy of Sciences, to conduct a proper epidemiological study.

C. All scientific research conducted by Federal agencies should be done without interference from Federal components outside their respective agencies

The White House made crucial decisions affecting the course of CDC's Agent Orange research, and the outcome. This kind of political interference is inappropriate and casts doubts on the integrity and credibility of Federal research. While components of the Federal Government should be free to make policy determinations based on Federal research, they must not be allowed to have policy determine the outcome of such research. The committee recommends that all scientific research conducted in the future by Federal agencies be done independently from the White House or other political organizations. If regulations do not already require such independence, then each agency should promulgate rules to prevent political interference.

Dissenting views of Hon. Richard K. Armey, Hon. Frank Horton, Hon. Howard C. Nielson, Hon. J. Dennis Hastert, Hon. Jon L. Kyl, and Hon. Chuck Douglas

Agent Orange is a highly emotional and controversial issue with strong political pressure for answers. We have deep sympathy for veterans and their families who believe their suffering is due to Agent Orange exposure, and we want the record to be clear that we remain committed to compensating American veterans for service-connected disabilities.

Regrettably, however, instead of advancing the debate on Agent Orange in a positive direction, the Human Resources Subcommittee has abused this issue in order to launch an ideological assault upon a Republican White House with which it has never agreed. Consequently, constructive suggestions for further review and detached review of science are given a back seat to unsubstantiated charges of a political coverup, and the Committee Report seems more concerned with writing the President out of the Constitution than it does with evaluating the science surrounding Agent Orange. Our view is buttressed by the Subcommittee Chairman's steadfast refusal to rethink his charges against the White House and work with us to develop an Agent Orange report that all members of this Committee could support. In fact, the draft report was already printed in final galley form by the Government Printing Office before minority members were ever given a copy.

Our concerns are not limited to procedural grounds, however, and we have many specific reservations with the report. In addition to being highly emotional and controversial, studying Agent Orange is also an extraordinarily complex task, and these enormous complexities cannot be as readily dismissed as they were by the Committee Report. The fact is that while CDC was charged with studying the exposure of Vietnam veterans to Agent Orange, determining exposure is just not as easy as it sounds. For example, when we refer to exposure, do we mean opportunity for exposure or actual exposure to Agent Orange. The distinction is crucial.

If we're referring to actual exposure, several additional factors come into play. What was the quantity of the exposure? How long was the veteran exposed? Was exposure on the skin or clothes? How long did exposure occur after spraying? Was the exposure repeated? The answer to these questions were important factors in the National Cancer Institute studies cited by the Committee Report to substantiate the link between herbicides and certain cancers. Good science suggests that these questions should not have been ignored in the Agent Orange study. Furthermore, the answers to these questions are extraordinarily difficult to ascertain twenty years after actual exposure. Consequently, when we recognize that the CDC study was premised upon determining actual exposure,

and after CDC made several attempts to accurately determine exposure, CDC's conclusion that a scientifically valid exposure study could not be done is not as dubious or devious as some would suggest.

Conversely, if you're conducting an exposure opportunity study as the Committee Report implies the CDC should have done, you invite serious misspecification errors which could render further study useless. Misspecification means that we identify persons as exposed when they were not exposed and vice versa. CDC was reluctant to use this approach because it believed it would be a disservice to veterans to measure the existence or non-existence of health effects on persons who could not be conclusively determined to have been exposed to Agent Orange.

While proponents of an exposure opportunity study readily admit that this approach creates an opportunity for misspecification, they downplay this concern by asserting that these errors will cancel each other out; however, this is not an acceptable response. Epidemiologists who argue that misspecification errors will cancel each other out are guilty of using the statistician's equivalent of the punt. There is no scientifically justifiable explanation for asserting that misspecification errors are random, and the cancelling out argument is nothing more than a convenient way to dismiss errors that can't otherwise be explained away.

The bottom line is that any study put together by CDC would be subject to legitimate attack for its shortcomings. In fact, we suspect that if CDC conducted an exposure opportunity study concluding that there is no relationship between exposure to Agent Orange and adverse health effects, the Human Resources Subcommittee would be the first in line to attack the very model it now supports because of its misspecification weaknesses.

The Committee Report's author would probably seek to refute our arguments by pointing to the independent National Academy of Sciences' (NAS) Institute of Medicine (IOM) report which raises the same criticisms as the Committee Report regarding the CDC's handling of troop data. However, this report is mischaracterized in the Committee Report and is inappropriately used to support the Human Resources Committee's political conclusions.

On July 19th, Institute of Medicine President, Samuel Thier, responded by letter to an article appearing in the July 23rd issue of Time Magazine (Time reaches the newsstands before its published date) entitled "A Cover-Up on Agent Orange." This article reported similar coverup and manipulation charges as those raised in the Committee Report. However, in his letter, Dr. Thier says that the Time article,

> incorrectly says CDC suppressed a 1986 report from the Institute of Medicine (IOM) of the National Academy of Sciences. The document in question was actually an internal report . . . [and] the report did not criticize the CDC study; it was about the Defense Department, not the CDC.

More important, however, Dr. Thier asserted that the report concluded,

> [The] Defense Department was capable of handling troop data, *but also expressed concerns that these might not be accurate measures of exposure to Agent Orange.* [Emphasis ours.]
>
> The 1987 IOM pre-publication review of CDC's Agent Orange Validation Study was critical of the CDC's work because the committee was explicitly asked to critique the agency's draft report. However, *the IOM report also states that the CDC design, methods and analyses were well conceived, appropriately executed, and clearly presented.* [Emphasis ours.]

Unfortunately, the Committee Report does not end with its criticisms of the CDC study, but chooses to extend its outrageous accusations of coverup to the Reagan White House.

After subpoenaing virtually every imaginable document prepared, reviewed or witnessed by the White House regarding Agent Orange, the most the Committee Report can tell us is that the White House opposed legislation which presumed that simple exposure alone to Agent Orange constituted a service-connected disability meriting compensation. We are then asked to conclude that this opposition provided the impetus for its plot to cover up the truth about Agent Orange. This conclusion is simply not supported by the facts

First, we need to acknowledge that compensating veterans for simple exposure to Agent Orange is a political decision, not a scientific one. Scientific information made available to the White House, from both inside and outside of government, has failed to establish any supportable conclusive link between simple exposure to Agent Orange and adverse long-term health effects. Therefore, the practical effect of the White House's legislative position was to oppose spending billions of tax dollars to compensate for an event that virtually no scientist has linked to long-term disabilities

Consequently, we find it highly ironic and extremely troublesome that while the White House is repeatedly attacked in the Committee Report for ignoring science and using political manipulation, when the White House makes a decision clearly supported by science, this decision is seized upon by the majority as the key evidence supporting a political coverup. We wonder who's the real one playing politics.

Next, we find it totally implausible for the White House to mastermind a coverup on its own when Congress was intimately involved in the Agent Orange proceedings since their inception. The Office of Technology Assessment (OTA) and the House Veterans Affairs Committee under the able leadership of its Chairman Sonny Montgomery had either participated in or had overseen the progress of the CDC study, and both supported the CDC's activities and conclusions.

In a House Veterans Affairs Subcommittee press release dated March 29, 1990, Chairman Montgomery is quoted,

> Agent Orange has been and remains an emotional and controversial issue, but the findings of [the CDC] and all reputable studies are convincing: There is nothing to show

decisively that there are long-term adverse health effects as a result of exposure to Agent Orange.

Regarding the report prepared by Admiral Zumwalt and relied on so extensively by the Human Resources Subcommittee, the OTA had this to say in a July 23rd, 1990 letter from John Gibbons to Congressman Montgomery,

> The report seems to take the form more of a legal brief than of a scientific review of evidence. . . . Based on a review of the areas in which OTA has been involved, we conclude that many of the assertions made in the report supporting a conclusion that Agent Orange is responsible for a wide range of health problems among Vietnam veterans, are incorrect. These are not mainly matters of differing opinion, but matters of fact—what did or did not happen. For those aspects about which OTA staff have detailed knowledge, it appears that Admiral Zumwalt's arguments are based, in many instances, on faulty information or incorrect interpretation of data.

Therefore, the Committee Report cannot accuse the White House of engineering a coverup without also implicating Congress and several highly respected members of this body, and we refuse to do so. Charging Members of Congress for a coverup is simply ludicrous, and so is charging the White House as well.

We suspect that the real motivation behind the Human Resources Subcommittee Chairman's zealous attack on the White House is to lay the groundwork for his final recommendation and real goal: writing Republican Presidents out of the Constitution. By recommending that all scientific research conducted in the future be done independently from the White House or other "political" organizations, this goal is made clear.

However, the last time we looked, Article II, Section I of the Constitution of the United States still vested executive power in the President of the United States. Notwithstanding the desires of the Committee Report's authors, we are unaware of any Constitutional Amendments to change this "political" office.

This final recommendation of the Committee Report is most troubling because it highlights an ongoing double standard applied by the Human Resources Subcommittee regarding the work of scientists, both inside and outside of government. The implications of this double standard are clear: If you're a scientist who agrees with the political conclusions of the Human Resources Subcommittee Chairman, your views will be put forth as gospel, and no one has a right to question them. On the other hand, if you're a scientist who disagrees with the Chairman's political conclusions, you'll either be lucky enough to be ignored, or you'll face the unfortunate prospects of having your views attacked and your integrity questioned before a publicly held Congressional hearing.

We are simply tired of seeing Administration officials constantly dragged through the Human Resources Subcommittee wringer under the banner of science over politics, when the Subcommittee is the one so clearly guilty of playing politics itself.

Veterans deserve much better than what this report seeks to offer.

RICHARD K. ARMEY.
FRANK HORTON.
HOWARD C. NIELSON.
J. DENNIS HASTERT.
JON L. KYL.
CHUCK DOUGLAS.

Mr. ROHRABACHER. Thank you very much, Admiral.

I would ask—I will reserve my time until after the other Members of the Committee.

Former Chairman Brown, do you have some questions?

Mr. BROWN. Admiral Zumwalt, I think we all are aware of the fact that Agent Orange was not used as a means of creating disease or illness but was intended to be used as a defoliant and that it was the contaminant of dioxin that caused the problems that we have had.

At least we think it was that contaminant.

There may have been other contaminants, too, I suppose, that we don't know about.

But in your concern over Agent Orange, have you also reviewed the broader problem and its contemporary state that we are facing here with the ongoing concern about dioxin and its multitude of sources within the environment?

Admiral ZUMWALT. Yes, sir, I have.

And you are correct that we didn't know at the time that dioxin was a contaminant in the Agent Orange mix.

We know that the chemical corporations producing it knew at the time that it was carcinogenic.

It is also accurate, Mr. Chairman, that I have followed very closely the work of the EPA and have reviewed all the studies as they have come out.

And in my judgment, the EPA risk assessment was sound and scientific and objective, and the comments of the Science Advisory Board were the result of the presence on that group of representatives of industry.

Mr. BROWN. Well, I am sure the committee will want to review that, but this is an ongoing, this is a problem that extends far beyond dioxin.

We used to have a joke out in California that when we had a big oil spill that you couldn't find a petroleum geologist that didn't have a conflict of interest because they were all hired by the oil companies.

You have similar problems with asbestos, with breast implants, silicone, and other things of that sort.

I am not sure what the solution to that is, because frequently the most knowledgeable people are people who are hired by private industry and sometimes they can overlook these connections and contribute to a balanced judgment about it.

But this is going to be a problem in many areas for some time to come, as I am sure you realize yourself.

Admiral ZUMWALT. Yes, sir. I certainly agree with that.

One way, for example, in which a greater degree of objectivity might have been achieved today is if, in counterposition to the two doctors who have been subsidized by industry to a certain extent, you had in the hearing two scientists who had not.

Mr. BROWN. Admiral Zumwalt, I wanted to particularly get your views on the subject of a cooperative agreement with the Vietnamese Government to do a binational study in which each country will participate on the effects of Agent Orange and the dioxin component of it. And you have far more experience on that than most people have.

Do you think the time might be ripe not only to cooperate in resolving this or bringing more light to bear on this problem as well as in a more general sense establishing a research, cooperative research relationship with the Vietnamese as we do with many other countries, both European, Asian, and other parts of the world? Are we ready to go that far with the Vietnamese? And this is a subjective judgment, but I can't think of anybody whose judgment I would respect more on this than you.

Admiral ZUMWALT. Yes, sir.

In my judgment, we are.

I might report that with the assistance of Vietnam veteran Senator Harkin, we were able to get language in the appropriation bill a year ago that instructed NIEHS to do a joint research with the Vietnamese and the group that Dr. Lucier spoke about was the fruit of that language.

Following that, I went to Vietnam for my first visit since the war, in September of 1994.

I met with the former enemy general who is now president of the country, Le duc Ann, with General Giap, with General Tran Van Tra, who commanded the Viet Cong forces.

When I met him in Saigon, as an aside, I said, "General, I am surprised how easy it was to find you today. Twenty years ago I spent 2 years looking for you and never could find you."

He laughed and said he was in Tayninh province the whole time, that it's just as well we didn't meet, he said, or one of us wouldn't be here today.

[Laughter.]

All of those generals plus the minister of health and the doctors assigned to Agent Orange issues in Vietnam have pledged total interest in and cooperation for joint research on Agent Orange.

The Vietnam veterans strongly welcome that as a means for getting answers to the questions still unresolved about the 18 additional diseases that the VA has not yet authorized compensation for.

Mr. BROWN. It's conceivable that a broad study of the Vietnamese population who not only may have been exposed 20 or 30 years ago but whose children or maybe even grandchildren now might give us some information about mutagenic or teratogenic or other effects that would be extremely useful if we were to undertake that now.

Admiral ZUMWALT. Yes, sir. Absolutely. And in my judgment, Dr. Farland was in error in stating that we don't have highly exposed Vietnamese populations.

We do have villagers who were very heavily exposed.

The data that Dr. Farland has seen was compiled by Dr. Arnold Schechter, who was so limited in research funds that he had to take blood samples from a large group of people and then pool the blood and measure the dioxin in it, which made it impossible to know the individual high levels but just one average level.

Mr. BROWN. Well, I am very disturbed by—disturbed by our failure to move aggressively on an opportunity like this, and I am also convinced that successful arrangements for such a joint program would have immeasurable benefits in terms of our own understanding as far as our veterans are concerned and be very helpful to the

Vietnamese people, who probably also have suffered a great deal of disease from this.

I hope we can follow up on that aggressively in the future.

Admiral ZUMWALT. Thank you, sir.

Mr. ROHRABACHER. Thank you very much, former Chairman Brown.

Congressman Olver?

Mr. OLVER. Thank you, Mr. Chairman.

Admiral Zumwalt, you made a couple comments here, and I would like to clarify a little bit what you said toward the end of the testimony, and I was checking to see if it was written in exactly this form in your written form because I can sometimes, if I read things three times, understand them a little bit better.

But you said that the companies who produced Agent Orange knew that it was carcinogenic. Now, I don't know whether—or close to that, in any case.

Did you mean that they knew that it contained dioxin, which they knew was carcinogenic, or that even the broader Agent Orange is?

Admiral ZUMWALT. I have seen documents which show that there was knowledge within the chemical corporations that the processes they were using produced dioxin and that it was known that it had carcinogenic effects.

Mr. OLVER. I see. So you're saying that they knew that it contained, that it produced in the process of producing Agent Orange, that they knew that dioxin was in it and they also knew that was carcinogenic?

Admiral ZUMWALT. Yes, sir.

Mr. OLVER. All right. That clarifies that little point, in any case.

You made several comments about the Science Advisory Board, and your main recommendation here, I guess, is that the Science Advisory Board contain no scientists that have a financial interest in corporations.

The way your testimony speaks, you speak at one point of the Science Advisory Board reviewing EPA's draft assessment and then the Science Advisory Board review of EPA dioxin reassessment, there must be—I don't know, is that two different Science Advisory Boards? Did the—was there one? No, I guess that one would be the same one.

Admiral ZUMWALT. Yes, sir.

Mr. OLVER. But when you speak of—is this a Science Advisory Board created only for this particular draft assessment, reassessment of the dioxin effects? Or is it the EPA's broad Science Advisory Board?

Admiral ZUMWALT. I don't know the answer to that. I know that they were the board that did review this risk assessment.

Mr. OLVER. I think it would be very difficult to create a set of panels here that did not have some scientists who had some involvement, though I completely agree with you that if one has a panel set up to look at an assessment of dioxin's effect, that you should have nobody on it that is—that has a financial interest in the production of dioxin or in the production of the material, whatever its major purpose is, that contains within it the dioxin.

So, it maybe that this is a very subtle difference. But we have a longstanding history, at least in the judicial process, of judges and so forth recusing themselves from involvement in decision making where they have some interest.

From apparently what you say, you don't think that kind of an approach would apply?

Admiral ZUMWALT. It would be better than the current approach. During the writing of the Science Advisory report, observers close to the review process have identified Drs. Greenley and Graham as the two members of the Science Advisory Board health panel who most actively and consistently challenged the validity of the dioxin health risk assessments contained in the EPA report.

They were the panel members who pressed most vigorously and effectively for an outright rejection of the risk characterization section of the report, and yet they were the ones who have been subsidized by industry.

Mr. BROWN. Would the gentleman yield briefly on that?

Mr. OLVER. Sure.

Mr. BROWN. Admiral, you obviously have some documentation on this.

I am not familiar with it. But could you supply that for the record also?

Admiral ZUMWALT. Yes, sir, I would be glad to.

Mr. BROWN. And, of course, I would like to make the comment that all scientists, including my good friend Mr. Olver, are known to be totally objective about every subject and they don't have to recuse themselves from anything.

[Laughter.]

Mr. OLVER. Okay. Just trendy, however.

Staff has informed me in the midst of this that, in fact, it was a special subpanel and, of course, when put in the terms of a subpanel, then my mind says, well, is this a group of the overall panel? But I am now told that there is a science advisory panel of 39 members that sits there.

Now, in that science advisory panel, one I think ought to be able to expect scientists to recuse themselves from involvements in decisions where there is any kind of special interest.

I am not sure that you could find a scientific panel of 39 really top-notch scientists who haven't at one time or another or now have some interest in—in a particular scientific area that had some financial interest of a sort. Even the academic scientists, through their research contracts and so forth, may well have had that.

But when you create a subpanel for a particular reassessment, it seems to me that you are entirely appropriate by expecting that in that subpanel, which has one purpose, that there should be no scientists who have a financial interest in the outcome of the result.

They can take testimony from people on both sides. That's why we have panels here. You could have the two doctors in question on a panel to put their point of view forward and then there is a full—then you have a full opportunity to examine what they're saying and from that kind of conflicts of interest they might be coming in that process.

But at least they aren't there voting on and persuading others to the particular point of view, which I think really, really causes serious questions in what we're doing in our—in our reviews and in an objective way of developing scientific panel information.

Admiral ZUMWALT. Sir, I have two comments.

First, not only did Drs. Greenley and Graham not recuse themselves, they campaigned vigorously for and wrote the language that tended most to denigrate the EPA's panel risk assessment.

Second, in the case of the IOM study panel, Dr. Kenneth Shine was able to identify highly respected scientists who had not been infected by industry subsidies and when that was done, the science led to the objective conclusions that there were now 10 diseases that, likely as not, result from exposure to Agent Orange.

The difference between a panel which has industry representatives posing as objective and a panel which has none is like night and day when one compares those two results.

Mr. OLVER. Can you find, Admiral, can you find testimony or records that shows that, in fact, it was known by that panel at the time that the two that were making these—taking these positions were—did, in fact, have a relationship to the companies that were producing the Agent Orange contaminated with dioxin?

Admiral ZUMWALT. Well, yes. For example, in the transcript of May, Dr. Greenley has said and is quoted as saying, "Those of us for whom dioxin supports our family, sometimes we keep looking for problems that aren't necessarily there because it puts food on the table."

Mr. OLVER. Thank you, Mr. Chairman.

Mr. ROHRABACHER. Thank you, Mr. Olver.

Admiral, have you heard much about this ranch hands study?

Admiral ZUMWALT. Yes, sir. And I have examined it in fairly extensive detail.

Mr. ROHRABACHER. Maybe you could give us your opinion of that?

Admiral ZUMWALT. To go back, Mr. Chairman, the—at the time when, as the Government Operations Committee report shows it was government policy to instruct agencies not to find a correlation, there was a great deal of difficulty with the early Ranch Hand studies. And, for example, Senator Tom Daschle had to work arduously over a number of years to get released a study by Ranch Hand which was withheld because it showed that there were birth defects in statistically significant increased numbers.

When one compared the veterans before they went to Ranch Hand who had children with the equivalent control group, they had a normal rate of birth defects. When one compared their children that they had after they returned from Vietnam with a control group, they had elevated numbers of birth defects.

It took a long time to get that out, because it was being withheld.

The second point I would make is that not very much credence can be put in Ranch Hand, for two reasons, with regard to carcinogenic effects. The number of Ranch Hand personnel involved are too small to produce significant numbers. It's less than 1,200.

Second, one of the great fictions, in my judgment, about Vietnam is that the Ranch Hand group was the most heavily exposed. The Ranch Handers wore protective clothing. When they got back from

their spraying missions, they took the clothing off and took showers. The poor guys on the ground who were using Agent Orange themselves, my boat crews in their perimeters in the exposed areas, equivalent numbers in the Army and so forth, were much more heavily exposed. And therefore, one cannot put credence on Ranch Hand as being kind of the most exposed population.

Mr. ROHRABACHER. But you do concede that they are a heavily exposed population?

Admiral ZUMWALT. They are more heavily exposed than Vietnam veterans who did not go into combat. They are less heavily exposed than most who were actually in forward combat.

Mr. ROHRABACHER. All right.

I am in certainly no position to say one way or the other on that.

I will do some more reading on this issue.

However, today we were actually looking into process of evaluating——

Admiral ZUMWALT. Yes, sir.

Mr. ROHRABACHER. [continuing] rather than the actual outcome itself.

And your point which goes into your point about company docs, as you call them, in my—to my way of thinking, Admiral, and with all due respect, what you are doing is attacking the credibility of someone who opposes your view rather than attacking the validity of their arguments.

And quite frankly, you know, it is easier to attack the credibility of someone and attack someone rather than an argument, quite often in politics, and people move in that direction.

And I will say that there are, quite often, people who have—I don't—let's say they are a Catholic, well, they may be a Catholic and they may be absolutely committed to the Catholic religion, but that doesn't make their arguments wrong or that doesn't make their arguments irrelevant when it comes to, for example, abortion. And if it's wrong to say, well, you're a Catholic, that's why you're against abortion, rather than talk to someone and say, well, you're saying that life begins at conception and that's how we have to make our judgment, let's look at that argument.

It seems to me that that's not the proper way to try to determine the truth, and the idea is to determine the truth, attacking the arguments rather than attacking the people.

Go right ahead and respond to that, sir.

Admiral ZUMWALT. You know, it's distasteful for me to have to make those points. The veterans have for 15 years seen the manipulation of studies. It has been documented that the studies were manipulated. We know that it was done by industry interest groups. And the veterans—

Mr. ROHRABACHER. I am not suggesting that's not true. It's very possible that you're accurate on that.

Admiral ZUMWALT. All right.

Mr. ROHRABACHER. But when you're talking about government panels like this, for example, where you said we had two witnesses who had received certain support for their research in the past or even in the present from business, that they should be excluded.

Admiral ZUMWALT. Yes, sir. And I am sure that my years in the military have made me more—less diplomatic and more accurate.

Mr. ROHRABACHER. No, no, that's fine.

[Laughter.]

Admiral ZUMWALT. The—no mention was made of the tremendous conflicts that these two gentlemen have. Surely, at some point in the hearing it's appropriate.

Mr. ROHRABACHER. Well, Dr. Farland, for example, is the head of the EPA, and he certainly has every reason to try to present the best arguments for his—for the EPA, for the bureaucracy that he oversees.

Admiral ZUMWALT. I think Dr. Farland's mission in life is to come up with scientifically objective data, whereas the mission in life of the industry representatives is to reduce the exposure of those industries.

Mr. ROHRABACHER. Now, are you presupposing that people who have worked for industry then cannot be honest people?

Admiral ZUMWALT. There are some who are honest.

Mr. ROHRABACHER. Well, let me put this more in your own—in your own back yard.

By the way, I would never say that of anybody else, some are honest. I would never presuppose that people are not being honest in their disagreement with me, even on really gut issues.

Let me put it to you this way. You are an admiral in the Navy. We have other committees that meet in determining major expenditures for the United States Government.

Now, who do we call as witnesses when we are trying to make those determinations?

Well, I bet you probably testified. But you're an admiral.

Admiral ZUMWALT. Yes, sir.

Mr. ROHRABACHER. And your whole life came from money coming from—to the Navy. Now, does that mean that we shouldn't have military people here to advise us because they have—and we all know about the conflict between the Navy and the Army and the Air Force over where the funds should go.

Shouldn't we have people from the military here who have the expertise to give us that testimony?

Admiral ZUMWALT. Oh, absolutely they should be there.

When I came in and testified, I identified myself as chief of naval operations and, therefore, responsible for and obviously in favor of the budgets that I submitted.

Dr. Jones did not come in and identify himself as someone who has lobbied for and represented the Incinerator Association.

I think those—that is the difference that I am referring to.

Mr. ROHRABACHER. Okay. I think that that's fair to say that people who testify, that their backgrounds should be available to the public.

I think that's fair. But I don't think it's fair to say that because someone has worked for industry, whether it's the incinerator burners or someone else, that they shouldn't be able to testify and their arguments shouldn't be considered.

Mr. OLVER. Would the chairman yield for a moment?

Mr. ROHRABACHER. Well, first let the admiral answer that, and then I will be very happy to yield to my colleague from Massachusetts.

Admiral ZUMWALT. Yes, sir. I would assert, in that regard, that there is widespread recognition among those scientists who do not take subsidies from industry that there are a subset of scientists who do and, therefore, come up with unobjective conclusions.

Mr. ROHRABACHER. Well, Admiral, I am not certain that this is an area of your expertise, and I will say that there are people who are hired as consultants in any number of areas and it does not mean that they cannot get the honest individuals and give honest testimony, and if someone, for example, does some scientific research and finds something that backs up the arguments of a particular industry, quite often the industry moves forward to try to help supplement that research.

That is in—that is something that is very natural. That doesn't mean people are lying along the way. That just means that that's the natural outcome.

For example, if the Navy was going to get cut off from a certain amount of funding, the Navy might subsidize someone, a Ph.D. who was doing a study that the Navy knew would show that naval power was important, but that doesn't mean that researcher is lying about the importance of naval power.

Admiral ZUMWALT. I certainly understand that point you're making.

On the other hand, I would point out that I think it is generally recognized now that the tobacco industry has been deceiving the public for years and that their scientists have been cooperating with them in doing so.

Mr. ROHRABACHER. All right. Well, you see, I disagree with that point.

I think that anybody, anybody in their right mind has always known that tobacco is bad for you. And from the time I was a little kid, common sense and everybody from my church to school, everybody else was saying cigarettes, they used to call them coffin nails, and the tobacco industry, for them to be suggesting that, "Oh, we didn't, you know," to say that they in some way were trying to cover up the fact that it was bad, they were selling a product just like alcohol and a lot of other things that have—that are bad for your health but people have the right to make the choice.

Admiral ZUMWALT. Yes, sir, but there are scientists who practice voodoo science in asserting that the tobacco companies were right.

Mr. ROHRABACHER. I think that those—I think anyone who is hired by a private company or has an interest, whether a financial interest that makes them less than honest about the conclusions, about conclusions of their studies or less than honest in their decision making, those people are doing something that's wrong.

But that doesn't mean that all people who are engaged in research and are hired by private industry all of a sudden cannot be honest about things that they have determined.

Admiral ZUMWALT. I agree one cannot write out a whole group.

Mr. ROHRABACHER. But I will say also, anybody who testifies here and if there is a conflict or if they are, for example, if they have an association, their background should certainly be know.

We certainly didn't try to cover anybody's background up. And if my staff didn't put that on a resume and there were groups' resumes or something that went out, I would apologize for that, but

certainly we didn't try to make someone appear to be what they weren't.

But I find that the people who testified, just because they have had some sort of contract, research contract or whatever, with others in the past, I have to look at the validity of their arguments.

I can't just attack their credibility and try to attack them as a person.

Mr. Olver, would you like to jump in? You had something to say?

Mr. OLVER. Yeah. I almost feel completely obfusticated from the previous——

Mr. ROHRABACHER. Well, that's a tough one.

Mr. OLVER. [continuing] set of comments.

But in any case, I think the analogy isn't exactly as you have given it, Mr. Chairman. What we had here was not people asked to come in and testify where you could—where you could explore what their interests were and knew it when they came in.

But you had people who were actually in the panel that was supposed to be making a quasi-judicial decision to try to come up with the best scientific decision that would be possible, given the best that you know at that time and be as objective as possible.

It seems to me that——

Mr. ROHRABACHER. Well, I was just referring to the panelists today, Mr. Olver.

Mr. OLVER. Well, but your comments were related to who is there versus who is here.

We serve in a quasi—we are trying to look for the best circumstance, presuming that none of us are exactly experts in these areas, and all of us may have our own particular interests in it.

But in this case, where the integrity of the process, it seems to me, is enormously important, it should be cleaner than a hound's tooth, in essence, in order to be able to—for the people, for our constituents to believe that in fact it has been as objective as the science can allow it to be.

Mr. ROHRABACHER. If cleaner than a hound's tooth means that you don't permit people and certain arguments to be presented by the most——

Mr. OLVER. That's not what we're saying at all.

Mr. ROHRABACHER. But if that is——

Mr. OLVER. You're taking testimony from there. What I am suggesting——

Mr. ROHRABACHER. But if that is the result, Mr. Olver.

Mr. OLVER. I am not suggesting that that's the result at all.

We take the testimony from there and everybody on all sides gets heard.

But the panel who is supposed to make an objective decision on it should start out at least without clear conflicts of interest within it.

Mr. ROHRABACHER. Okay.

Mr. Olver, thank you for that point.

Admiral, we have about six minutes to go and vote. I want to thank you very much.

As you can tell, it was very provocative testimony because you have ignited a debate even here on our committee. And I want to thank you very much for your testimony today. I want to thank you

very much for the service that you have rendered our country, and your men, we all deeply respect. Thank you, Admiral.

Admiral ZUMWALT. Thank you, Mr. Chairman.

Mr. ROHRABACHER. This hearing is adjourned.

[Whereupon, at 2:00 p.m., Wednesday, December 13, 1995, the Subcommittee was adjourned.]

[The following information was received for the record:

6404 E. Halbert Rd.
Bethesda, MD 20817
December 29, 1995

Mr. Larry Hart
Subcommittee on Energy and Environment
B-374 Rayburn HOB
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Hart:

Thank you again for your interest and advice during the preparation of my material for the hearing on the "dioxin reassessment." I have edited the transcript of my remarks and returned them to Ms Disharoon. Mr. Rohrabacher stated that the hearing record would remain open, and I am using this letter to provide you with some additional comments.

1. As I remarked at the hearing, I believe the Air Force study of the Ranch Hands provides an enormous amount of information about men who were exposed to 10 to 100-times as much dioxin as the average person, the exposures at which EPA predicts an array of adverse effects. Moreover, I think that there is an effort to discount the results of that study because they do not support the claims made by many people about dioxin and Agent Orange.

a. The Air Force study finds no clinically significant differences between the Ranch Hands and the Comparisons, and no dioxin-related increase in death or disease in the Ranch Hands (Public meeting of the Ranch Hand Advisory Committee, Philadelphia, February 14, 1995, and the complete report is under review for public release). The Air Force study provides no support for the many claims of health impacts from moderate exposures to dioxin and none for the EPA's projections that more highly exposed people in the general population are suffering disease because of dioxin.

b. The Air Force has published the results of investigating every pregnancy of wives and lovers and every miscarriage and live birth of children born to the Ranch Hands and the Comparison group. The publication also reports the results of investigation of every birth defect and developmental defect in the children of the Ranch Hands and Comparisons through the age of 18 or so. No increase in any reproductive health event can be associated with dioxin (Wolfe *et al.* 1995. *Epidemiology* 6:17-23). The study, as an earlier study of the children of veterans of the ground war in Vietnam (Erickson *et al.* 1984. *Journal of the American Medical Association*

252:903-912), provides no support for the oft-repeated claim of elevated birth defects in the children of Vietnam veterans. They also offer no support for the reports of increased birth defects among children born to members of the North Vietnamese Army who served in South Vietnam during the war.

2. There was some discussion of the possibility of studying possible health effects of dioxin in Vietnamese populations. I regard this as unlikely to be worthwhile for three reasons.

a. The studies of Vietnam veterans in the United States have taken years to do and have cost hundreds of millions of dollars in the country with the best medical care system in the world. How much more difficult and more expensive will such a study be in a country with much poorer medical services and few records from the war period? I think that those difficulties will cause great reliance on recall about exposures, causes of death, past illnesses, and impossible problems in making accurate counts of live births, still births, and miscarriages.

b. There is no reason to believe that many Vietnamese were exposed to high levels of Agent Orange and dioxin except for the men who worked around the Ranch Hand bases or with U.S. Army Chemical Corps units, and those men would have exposures no greater than those of the Ranch Hands. The published measurements of dioxin levels in Vietnamese civilians are far lower than those in Ranch Hands and male worker populations and in the population of Seveso, Italy, where men, women, and children were exposed as a result of a chemical plant accident in 1976. [There is no indication of adverse effects in the Seveso population except cases of chloracne and two reports of increases in certain cancers that are based on very small numbers, that must be regarded as tentative, that make no sense from dose-response considerations, and that don't fit into the picture of cancers that might be associated with exposures to dioxin in the exposed workers.] Since elevations in disease rates are not apparent in the higher exposed populations, there is no reason to expect any in the Vietnamese.

c. Admiral Zumwalt stated that some new samples of blood from Vietnam contained much higher levels of dioxin. So far as I know, there is no published report of that. I also understand that the blood samples were held at an airport in Vietnam by Vietnamese officials for several days after they were collected. If the concentrations are indeed high in those samples, I would entertain the idea that they had been "spiked" during the time they were not in custody of U.S. officials. This could be checked by obtaining new samples and maintaining custody during the transport back to the United States. Such guarantees of non-tampering are standard forensic and scientific practice.

3. Admiral Zumwalt made many statements about what is known about dioxin that warrant comment, but I will mention only two.

a. He said that he had seen chemical company documents that indicated the companies knew that dioxin was carcinogenic when the companies were selling Agent Orange to the government. As I understand it, the use of Agent Orange was discontinued in 1970 following a 1969 report that dioxin caused birth defects in laboratory animals and a number of congressional hearings (Gough 1986. *Dioxin, Agent Orange*. Plenum Press. ch. 3). The definitive study that showed dioxin causes cancer in animals was not published until years later (Kociba *et al.* 1978. *Toxicology and Applied Pharmacology 97*:133-140).

The admiral may be mistaking the fact that the companies knew that high exposures to dioxin caused chloracne (Gough 1968. ch 13) with his contention that they knew dioxin was carcinogenic. If not, he has important information that should be made public.

b. Admiral Zumwalt said that "combat veterans" of Vietnam were more highly exposed than Ranch Hands. There is not a shred of evidence to support that assertion, and everything that is known refutes it (Centers for Disease Control Veterans Health Study. 1988. *Journal of the American Medical Association 260:*1249-1254; Kahn *et al.* 1988. *Journal of the American Medical Association 259*:1161-1667; see Gough. 1991. *American Journal of Public Health 81:*289-290).

4. I disagree completely, as everyone would expect, with the value that Admiral Zumwalt places on the Institute of Medicine "study" that associated exposures to Agent Orange with several cancers. The IOM study was hardly mentioned during the EPA's May meeting about the dioxin reassessment, and the EPA does not rely upon it in any way in the reassessment. Indeed, the IOM conclusions differ so much from almost everyother set of conclusions about Agent Orange and dioxin that they must be regarded as significant outliers. [I will address the IOM report in the book that I am currently writing.]

5. Finally, I have some comments about Admiral Zumwalt's praise for the IOM panel that contained only people who professed ignorance of dioxin research at the time they were chosen and that excluded experts from chemical companies.

a. Advisory committees are made up of busy people with (typically) demanding jobs and professions, and serving on a committee or panel is a part-time affair, worked into a crowded schedule. Committees and panels generally are composed of experts to reduce the time and effort necessary to bring everyone up to speed. As a practical matter, non-experts depend on the staff of the committee or panel for much of their information, and I think that staff have too much opportunity to influence panels and

committees without experts in the area of study. Certainly, in all my years at OTA, I never heard of a panel of non-experts, and I don't know what it would be like to staff one, but I think it would offer a lot of temptation.

b. Admiral Zumwalt said that company experts should be allowed to testify before committees or panels but that they shouldn't serve on them. I think that to follow his suggestion would be to deprive certain people, because of their associations, with what I regard as their constitutional right to advise their government. If the sad history of the 20th Century teaches us anything, it is that accepting or rejecting individuals as "worthy" or "fit" based on their associations is a doorway to abuse.

Admiral Zumwalt appears to regard panels and committees as decision-making bodies; they are not. They don't make policy decisions; they advise elected or appointed officials who do. If they are making decisons, then, indeed, we need to look closely at the system, but the necessary repair is not to be found in denying membership on the basis of associations.

["Conflict of interest" can be seen and balanced. If conflict of interest is sufficient reason to deny membership to a company expert, it should also be sufficient reason to deny membership to representatives of environmental organizations. The frequent lawsuits brought by such agencies against the Federal government represent a clear conflict of interest.]

I hope that you had the happiest of holidays and that the new year is very good for you. Please call if you have any questions or comments; my home phone is 301/229-3532, and my work phone is 202/789-5427.

Sincerely,

M. Gough

Michael Gough

CHLORINE CHEMISTRY COUNCIL

A
Council
of the
Chemical
Manufacturers
Association

December 18, 1995

The Honorable Dana Rohrabacher
Chairman, Subcommittee on Energy and Environment
House Science Committee
2320 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Rohrabacher:

On behalf of the Chlorine Chemistry Council, I appreciate the opportunity to submit these comments to the record for the dioxin reassessment hearing held on December 13, 1995. Please do not hesitate to contact me if you have any questions.

Sincerely,

C. T. "Rip" Howlett
Managing Director
Chlorine Chemistry Council

Chlorine Chemistry Council • 2501 M Street, NW Washington, DC, USA 20037 • Tel. 202-887-1100

CHLORINE CHEMISTRY COUNCIL

A
Council
of the
Chemical
Manufacturers
Association

CHLORINE CHEMISTRY COUNCIL
STATEMENT TO THE HOUSE SCIENCE COMMITTEE
SUBCOMMITTEE ON THE ENERGY AND ENVIRONMENT

SCIENTIFIC INTEGRITY AND THE PUBLIC TRUST
THE DIOXIN REASSESSMENT

The Chlorine Chemistry Council (CCC), a business council of the Chemical Manufacturers Association, supports the Environmental Protection Agency's efforts to reassess the sources of dioxin exposure and the effects of dioxin on human health. CCC has submitted extensive comments to EPA and its Science Advisory Board (SAB) on the draft Reassessment. In those comments, CCC highlighted other scientific studies and different interpretations of the critical literature cited by EPA.

CCC mainly agrees with the conclusions of the SAB regarding the draft Dioxin Reassessment's Dose-Response and Risk Characterization chapters, and believe the Agency should take the substance of the SAB's comments into careful consideration. We endorse the SAB recommendation that Chapters 8 and 9 be redrafted in a reasonable and timely manner. The rewrite process begun by the Agency, as evidenced by its December 8, 1995, stakeholders meeting, is a good start.

We support the open process in which the draft Reassessment is being reworked and look forward to meaningful participation by scientific experts from a number of disciplines and from across government, industry, environmental organizations and others. A scientific peer review is critical to the credibility of the reassessment. We will continue to work with EPA in finalizing the document.

Chlorine Chemistry Council • 2501 M Street, NW Washington, DC, USA 20037 • Tel. 202-887-1100

Zephyr Consulting

January 17, 1996

Honorable Dana Rohrabacher
Chairman
Energy and Environment Subcommittee
U.S. House of Representatives
Suite 2320, Rayburn House Office Building
Washington D.C. 20515- 6301

Dear Congressman Rohrabacher,

It was indeed my pleasure to have the opportunity to testify before your committee on December 13, 1995 regarding the scientific integrity of EPA's dioxin reassessment. I hope that my comments were insightful.

When I reviewed the testimony record I noted that Admiral Zumwalt, who doesn't know me, went out of his way to impugn my testimony and my professional integrity. I have written a letter to the Admiral challenging the statements he made in this regard. This self explanatory letter along with appropriate attachments are appended to this transmittal letter. I would greatly appreciate having this correspondence made a part of the hearing record. Hopefully, it will remove the tarnish that Admiral Zumwalt so blatantly cast upon my professional reputation.

Respectfully,

Kay H. Jones, PhD
Capt. USPHS (retired)

cc. Admiral Zumwalt (retired)

(206) 328-1615 • 2600 Fairview Ave. E., Suite 18, Seattle, WA 98102

Zephyr Consulting

January 3, 1996

E.R. Zumwalt Jr.
Admiral USN (Ret.)
Chairman Agent Orange Coordinating Council
1000 Wilson Blvd., Suite 3105
Arlington, VA 22209-3901

Dear Sir:

I am deeply disturbed by your derogatory remarks impugning my character and honesty which you made before the House Subcommittee on Energy and Environment, Dec. 13, 1995. As a retired senior officer retiree with 20 years of service in the USAF and USPHS, I have always upheld the military code of ethics of being an officer and a gentleman at all times. I am committed to the same code of conduct which my daughter is held to as a recent graduate of the U.S. Air Force Academy (class of 1995).

Without any personal knowledge of my background and distinguished government service (see resume attached) you made the following direct and indirect personal attacks during your testimony

1. " a greater degree of objectivity might have been achieved today is if in counterposition to the two doctors who have been subsidized by industry to a certain extent..." (lines 2573, 2574)

2. "Yes sir. And I am sure that my years in the military have made me more--less diplomatic and more accurate." (lines 2876-2878.)

3. "-- no mention was made of the tremendous conflicts that these two gentlemen have. Surely at some point in the hearings it's appropriate" (lines 2881-2883)

4. "...whereas the mission in life of the industry representatives is to reduce the exposure of those industries " (lines 2889-2891)

5. "There are some who are honest." (line 2894)

6. "Dr. Jones did not come in and identify himself as someone who has lobbied for and represented the Incinerator Association" (lines 2921-2923)

7. "that there are a subset of scientists who do and, therefore come up with unobjective conclusions." (lines 2940-2942)

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Admiral Zumwalt, you have made false, direct and indirect accusations as to my professional integrity without foundation. For the record:

1. I have never lobbied for or represented the Integrated Waste Management Association (IWSA) or any other incineration related association.

2. I received a modest contract from the IWSA to review certain portions of the dioxin reassessment, i.e., related to background levels of exposure emissions sources and risk assessment methodology. The full text of my contribution which was submitted to the EPA peer review docket is attached. Other consultants who received funding from the IWSA included the renowned Swedish scientist Dr. Christopher Rappe. Do you also question his integrity? Please note that my findings about the decrease in the likely magnitude of the the unknown sources of dioxins would place more emphasis on incineration sources, not vice versa.

3. My professional area of expertise with respect to dioxins has focused on risk assessment of all forms of waste incineration emissions. The funding for such consulting work comes almost entirely from local governments or public solid waste authorities. In the cases where funding came from a vendor it was because the permitting costs were a part of the overall vendor/ authority project contract. In all cases my firm's (or my previous firm, Roy F. Weston) work products were thoroughly peer reviewed by State or local regulatory authorities. All such work products were in compliance with Federal, State and local permitting and/ or risk assessment guidance.

4. In my opinion, the greatest test of scientific credibility occurs under oath and in a court of law when appearing as an expert witness. I have stood this test on many occasions. I fully expected to have taken the oath prior to testifying on Dec. 13 which has been customary in other similar hearings. I am sure you would have tempered your accusations/ remarks had you been under oath.

5. I was not sponsored by the incinerator industry to testify on Dec. 13, nor did the industry have any prior knowledge of the content of my testimony.

I have almost 40 years of experience in the field of protecting human health and the environment, regardless of my tenure in the government, academia or private sector. I am fervently dedicated to seeing that good science leads to sound environmental policy. It shocks me that a retired Naval Officer of your stature would attack a fellow officer in such a blatant and dishonest fashion.

With All Due Respect,

Jay H. Jones, Ph.D.
Capt., USPHS (retired)

cc: Honorable Dana Rohrabacher
Chairman of the Subcommittee

Zephyr Consulting

KAY H. JONES, Ph.D.

EDUCATION

Ph.D. in Sanitary Engineering, (with minors in Chemical Engineering and Environmental Toxicology,) University of California at Berkeley, 1968

MS, Sanitary Engineering, University of California at Berkeley, 1961

BS, Civil Engineering, University of Washington, 1956

EMPLOYMENT HISTORY

1990 - present	President Zephyr Consulting Seattle, Washington
1981 - 1990	Vice President and Practice Leader for Air Quality Management Roy F. Weston Inc., West Chester, PA and Seattle, WA
1979 - 1981	Professor of Environmental Engineering and Deputy Director of The Environmental Studies Institute Drexel University, Philadelphia, PA
1975 - 1979	Senior Advisor for Air Quality Council on Environmental Quality Executive Office of the President Washington D.C.
1974 - 1975	World Health Organization (WHO) Consultant Ministry of Environment, State of Israel
1967 - 1974	Senior Technical Advisor and Research Manager Office of Air Programs, National Air Pollution Control Administration (DHEW) and U.S. Environmental Protection Agency (EPA), Washington D.C.
1959 - 1966	Bioenvironmental Engineer Biomedical Science Corp, U.S. Air Force
1956 - 1959	Civil Engineer, U.S. Air Force
1956	Civil Engineer, Standard Oil Company of California

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FIELDS OF COMPETENCE

Air quality management, air pollution control engineering, risk assessment, government affairs and policy analysis, litigation and expert witness support, public participation, international program development, research management, industrial hygiene, radiological health, teaching.

EXAMPLES OF PROFESSIONAL ACCOMPLISHMENTS

- Project director on many major industrial permitting projects, including one of the world's largest complexes, General Motor's SATURN plant in Tennessee.

- Directed several major projects involving the assessment of air toxics impacts of Superfund sites and hazardous waste disposal sites. Such assessments involved ambient monitoring, modeling, and risk assessment. Retained as expert witness for some 200 industrial defendants in major tort case involving a controversial Superfund site in Southern California.

- Recognized national authority on health risks associated with combustion of municipal and hazardous wastes. Directed risk assessment studies on 33 proposed projects and was technical advisor and or expert witness on 20 additional projects. Responsible for developing and maintaining a one-of-a-kind worldwide data bank on emissions data for municipal incinerators. Authored numerous national and international papers on this subject. Developed innovative approach to involving the public in the risk assessment process.

- Developed and maintained the only national air quality data bank outside of the U.S. EPA for the Motor Vehicle Manufacturer's Association (MVMA). Prepared three annual air quality status and trends chapters for the President's Council on Environmental Quality (CEQ) annual report as a consultant to CEQ. Prepared and presented definitive studies on ozone nonattainment issues on behalf of the Clean Air Working Group (CAWG), a lobbying group, representing some 200 U.S. industries. Co-authored several technical papers on this work.

- Directed the conduct of several air quality studies that questioned the need for excessive air pollution control measures, in particular VOC controls, on behalf of local governments and industrial groups. Authored several papers challenging the need for auto I/M programs. Provided testimony on behalf of city governments to EPA and state legislative bodies.

- Directed two innovative projects involving potential adverse air pollution impacts of alternatives to conventional home heating. Carried out an in-depth study of indoor air pollution at an active home using kerosene heaters. Provided definitive testimony before the Consumer Products Safety Commission in defense of their safe use. Conducted a comprehensive policy analysis of the required and local air quality impacts of wood stove use for the Coalition of Northeast Governors.

- At CEQ authored the Presidential Initiative on Acid Rain contained in the president's 1979 environmental message. This initiative was the foundation of the Congressionally mandated National Acid Precipitation Assessment Program (NAPAP). Developed an independent data system and method for assessing the status and trends chapters of five CEQ annual reports to Congress. Developed computerized air pollution population exposure and risk models. Prepared and critiqued legislation and proposed EPA regulations.

- As a WHO consultant to Israel, established that nation's comprehensive air quality management program within the Environmental Protection Service. Conducted policy analyses on auto emission standards, ambient air quality criteria and standards, and stationary source air pollution control practices. Designed ambient monitoring programs for all major cities and assisted in the development of local air quality management agencies at the city government level.

- Managed research in the areas of stationary and mobile source emissions control, meteorology, chemistry, and physics at EPA and NAPCA. Coordinated intergovernmental and government/industry programs on common areas of research. Was agency focal point for coordinating all meteorological research activities and the establishment of specialized air-pollution-related meteorological observation programs throughout the U.S. Was vice chairman and chairman designee of the research programs sponsored by EPA/API/MVMA under the auspices of the Coordinated Research Council's (CRC's) Air Pollution Research Advisory Committee (APRAC). Established the first comprehensive long-range research needs regarding all forms of stationary and mobile-source combustion.

- Coordinated international programs on air pollution matters at EPA and NAPCA. Directed a major program as part of President Nixon's initiative in setting up the NATO Committee on the Challenges to Modern Society. This initiative led to the establishment of a common air quality management policy throughout NATO similar to the concepts and goals in the U.S. This project was the most resource-intensive international program ever undertaken by the EPA ($1.7 million). Was also director of the U.S./Soviet bilateral program on research on control of mobile source emissions.

- Directed all environmental protection programs at the U.S. Air Force missile launch complex at Vandenburg AFB, California. Responsible for protection of Air Force personnel and the public during launches of space vehicles involving highly toxic propellants and nuclear materials. Designed an innovative toxic waste disposal system.

- In addition to the two years as a full professor at Drexel, taught for three additional years as an adjunct professor. Also taught environmental engineering courses related to air quality management at George Washington and Howard Universities during the period 1970 to 1979 (adjunct associate professor).

PROFESSIONAL AFFILIATIONS

American Society of Civil Engineers

- Past chairman of the Environmental Engineering Division
- Past chairman of the Air Pollution Research Committee
- Past member of the Environmental Systems Policy Committee
- Member of the Air, Noise, and Radiation Committee
- President of Student Chapter, University of Washington

Air and Waste Management Association

Past member and past board member of the Federal Conference of Environmental Engineers

Tau Beta Pi Engineering Society

Chi Epsilon Civil Engineering Society

AWARDS

Outstanding ASCE Student Member, 1956
USAF Commendation Medal, 1966
USPHS Commendation Medal, 1974
USPHS Commendation Medal, 1976

IWSA's Comments on EPA's Dioxin Exposure Assessment Document
(Estimating Exposure to Dioxin-Like Compounds
Review Draft EPA/600/6-88/005/Ca -- June 1994)

I. EXECUTIVE SUMMARY

The Integrated Waste Service Association has spent considerable effort researching worldwide data on dioxin and related compounds, including travel to Europe where Association members met with leading experts in the field of dioxin research. IWSA's submission to EPA contains 19 separate reports on dioxin from the U.S., the U.K., The Netherlands, Germany, Sweden, and France. In addition, IWSA funded research by the leading international experts in this field to review and comment on the agency's findings.

The results of IWSA's work reveal a troubling fact: that the EPA ignored existing research and reports when formulating the agency's conclusions about dioxin. The information contained in the following submittal reflects exhaustive research by hundreds of scientists. In particular, the Netherlands, Germany, Sweden and France approached the issue of dioxin sources in a comprehensive manner, unlike the EPA. For example, these European countries identified and measured in the field the sources of dioxin in their countries. Whereas the EPA admits it cannot account for between 54% and 81% of the dioxin found in the environment, Europeans have balanced their dioxin budget.

Unlike the U.S. EPA, European environmental policymakers look to the future. Every country, except the U.S., that has tackled the dioxin problem focuses its efforts on identifying efforts taken now that will bring down dioxin emissions in the future; and efforts that need to be taken in the future that will further decrease emissions. Whereas the EPA highlights in its report and media releases that municipal waste combustors (MWC) represent 3,000 g TEQ/yr, the agency gives little thought to explaining that a small minority of older MWCs with less efficient pollution control equipment emit the majority of dioxin emissions. EPA buries in its Reassessment the fact that such older facilities will be closed or fitted with modern pollution control equipment. In fact, modern facilities are more than 100 times cleaner than these older units. In the near future, MWC emissions will be less than 50 g TEQ/yr nationwide. This is not speculation, but the cold fact of necessary compliance with the Clean Air Act.

Yet, EPA issued a misleading statement to the media claiming 95% of all known dioxin emissions come from combustion without explaining the agency's clear lack of knowledge of dioxin sources. The simple statement left the public with the mistaken impression that municipal waste combustors are the only source of dioxin. Nothing could be further from the truth. European nations provide their citizens with a comprehensive inventory of dioxin sources and their individual contributions to the dioxin budget, rather than lumping sources and issuing general statements.

Germany has identified more than 100 sources of dioxin. Professor Rappe cautions that the U.S. budget misses major sources of dioxin. The production of iron, wood burning, and the earlier use of pentachlorophenol all may be greater dioxin sources than older, less efficient MWCs. Dr. Stellan Marklund of the Institute of Environmental Chemistry at the University of Umea, Sweden, points out the glaring omission by EPA to test mobile sources under field conditions versus the testing to date done only in a lab. If Marklund is correct in his hypothesis that dioxin tailpipe emissions are much greater when cars using unleaded gasoline are driven in the winter when streets are covered with road-salt or in coastal communities, then EPA has greatly underestimated the dioxin contribution of mobile sources.

Dr. Kay Jones takes issue with EPA's statement that long-range transport accounts for dioxin deposition in remote areas of the U.S. He suggests an alternative, reasoned hypothesis that EPA chose to ignore: that dioxin concentrations in agricultural crops may be the result of local dioxin sources such as farm machinery, trucks, trains, and highway traffic.

Professor Rappe points to another fundamental problem in EPA's dioxin budget. In order to reconcile emissions and deposition, the congener patterns in emissions should be similar to the congener patterns in deposition. The dioxin measured at the stack has a distinct congener pattern. The dioxin measured in the soil has a distinct congener pattern. If we are to believe that what comes out of the stack is what we find in the soil, the two patterns should match. They do not. Professor Rappe points out that ambient air, soil, and sediment have a higher ratio of dioxin to furans, but municipal waste combustion emissions have a higher ratio of furans to dioxin. This finding clearly implies that the higher concentration of dioxin to furans in the environment cannot be explained by emissions from municipal waste combustors.

EPA's rigid model which predicts how emissions from a source travel, deposit and then become part of animals, plants, and humans is technically flawed and unacceptable in its present form. There is no discussion in the Reassessment that EPA has approved four different risk assessment models for use in predicting dioxin fate and transport. The model used in this report contains dramatic changes in a variety of factors without explanation. EPA has ignored its own guidance of focusing by focusing on the 99.9th percentile of risk. The result is that policy decisions stemming from application of this risk model are based on the potential harm to a fictitious person who eats, breaths and touches an unrealistic amount of dioxin.

In all, IWSA and the experts who reviewed the EPA Reassessment on behalf of the Association have provided the agency with more than 30 specific areas of concern with the risk model. For example, EPA chose an air model, COMPDEP, as the air dispersion model despite the fact that COMPDEP has never been peer reviewed by the modeling community nor withstood the test of time similar to other air models such as ISCLT or COMPLEX1. The agency has not provided information on how COMPDEP behaves in complex terrain nor taken into account that the wet deposition algorithm in COMPDEP is out of date. The shortcomings of the model must be corrected before embracing it.

Another comment concerns a set of approved chemical constants provided in the EPA Reassessment that ignores the range of acceptable values contained in peer review literature. EPA should explain how it chose the values cited in its document and how the uncertainty implicit in this range of values is to be incorporated into indirect risk methodology.

The effects of photodegradation are likely to be extremely significant when estimating dioxin exposure. The agency chooses to ignore photodegradation despite the strong suggestion by experts that photodegradation, as well as other degradation processes not discussed by EPA, are the major forces in determining long range transport and our background body burden matrix.

IWSA has spent considerable time and effort to provide EPA with meaningful, accurate, and carefully prepared comments to assist the agency. We hope that our work will be helpful, and that this submission is only the beginning of a cooperative effort to understand dioxin in a comprehensive manner.

Zephyr Consulting

DRAFT

INTRODUCTION

EPA has used estimated annual deposition rates to calculate the annual TEQ dioxin emissions for the continental U.S. and Alaska. The range of their estimate is 20,000 - 50,000 gm TEQ/yr. Of this amount EPA has only accounted for 9,300 gm TEQ/yr. (central estimate). EPA believes that the difference is due to uninventoried sources or recirculation of historical deposition. A critical review has been made of EPA's documentation regarding their findings. Three questions were set forth to focus this review, these being:

1. Are EPA's deposition estimates accurate based on the scientific evidence at hand?

2. Are the deposition rates in the U.S. on the average higher or lower than in European countries?

3. Does recirculation play a probable role in the fate and effects of current dioxin emissions?

The ensuing discussion is directed at answering these three questions within the framework of our current state of scientific knowledge and judgment.

REVIEW RESULTS

EPA has used a nationwide deposition flux rate of 2 to 6 ng/TEQ/m^2/yr to estimate the aggregate annual emissions from known and unknown sources. These endpoint estimates were synthesized from their review of the available literature (10 citations). Only 2 of the citations pertained to U.S. measurements or research. Only one of these 2 studies related to direct deposition measurements in the U.S. The other one relates to sedimentation rate estimates from a lake core sample. In addition to assigning the 2-6 ng/TEQ/m^2/yr range of deposition flux rates to the lower 48 states, they assumed a 1 ng TEQ/m^2/yr for Alaska based on a single measurement in Northern Sweden. Table 1 is a summary of EPA's interpretation of the data they cite.

It is important to see if EPA properly interpreted the literature they cited in Table 1 in arriving at their continental deposition flux range of 2 - 6 ng TEQ/m2/yr and remote flux rate of 1 ng TEQ/m^2/yr.

It is not clear why EPA would state that the low continental value "could be as low as 2 ng TEQ/m^2/yr (based on limited U.S. data)." They calculated the low value of 1 ng TEQ/m^2/yr from Koester & Hites and the TEQ equivalent of the 375 PCDD/PCDF

ng/m^2/yr from Smith et al.'s work is 1.75 ng/m^2/yr (Smith 1994). EPA provides no rationale as to why either of these observations would represent a continental average. There is also no explanation as to how they arrived at 6 ng TEQ/m^2/yr as an upper limit "(based on European data)."

EPA did not properly report the results of the long range transport modeling results of Van Jaarsveld and Schutter. The lower limit of deposition at the boundary of their 1,000 by 1,000 km grid was less than 0.5 ng TEQ/m^2/yr. These low flux areas were both predicted for land masses and open ocean to the north of the European sources. The real important data contained in this paper was apparently overlooked by EPA. First, the deposition gradients between the urban/industrial areas and rural/remote areas should have been applied qualitatively to the continental U.S. Most of the U.S. does not look like Northern Europe. Most of the U.S. continental land mass does not have upwind industrial regions, e.g., the plains states, the Southwest, the Rockies and most of the western states. EPA could have applied the acid rain model for the Northeast (which they developed) in the same manner that was the analog for the European analysis. Secondly, this paper presented compatible modeled deposition and air concentrations which would allow for predictions of deposition flux in absence of actual deposition measurements. The range of these ratios was 0.24 - 0.39 ng TEQ/m^2/yr per fg/TEQ/m^3 (mean = 0.29). Thirdly, but very importantly, the paper presented data on how localized total wet and dry deposition is relative to point sources, i.e., a greater than 10 fold deposition flux decrease in 10+ km from the source. Had EPA applied this relationship to their low end flux estimate of 2 ng TEQ/m^2/yr the implied ambient air concentration would be 6.2 fg TEQ/m^3. This value is only 36% of the level assumed by Lorber et al. in their most recent Dioxin 94 paper on background rural air to beef model validation (Lorber 1994).

Liebl et al.'s paper also contained more useful data than that reported in Table 1 by EPA. The same deposition flux to ambient ratio (similar to that determined from the Van Jaarsveld and Schutter modeling exercise) can be estimated. The average value for the three years of measured flux and ambient data in their rural area case is 0.056 ng TEQ/m^2/yr per fg TEQ/m^3. The rural with some industry included case ratio was 0.050 ng TEQ/m^2/yr per fg TEQ/m^3. The ratio for the 1992 industrial/suburban site case was 0.12 ng TEQ/m^2/yr per fg TEQ/m3 which again suggests that most deposition occurs close to the source of emissions.

There are other literature citations that EPA did not include in their review. Some examples follow. Kühn and Steeg (1993) reported agricultural area deposition fluxes versus distance from Hamburg. The fluxes were 4.5 ng TEQ/m^2/yr at 2 km and 0.9 ng TEQ/m^2/yr at 9 - 18 km from Hamburg. EPA did not discuss Czuczwa and Hites (1986) Lake Siskiwit sediment data in this section of the report relative to atmospheric deposition rates in supposedly remote areas. Had EPA done so and assuming the total PCDD/PCDF to TEQ ratio was similar to that observed by Smith et al., they would have reported a deposition flux estimate of 1.09 ng TEQ/m^2/yr. Several soil deposition studies were overlooked by EPA which reflect both the gradients in atmospheric concentrations and deposition flux. Boos et al. (1992) measured soil PCDD/PCDF data at 24 diverse sites in Austria. Samples were analyzed for a variety of settings. The remote rural background level was about 1/30th of

the soil PCDD/PCDF concentration near urban areas. Measured levels near specific industries known to be dioxin emitters did not show levels above those associated with the urban emissions in general. These data again appear to conflict with EPA's assumptions that rural ambient concentrations are 1/5th of urban levels even assuming equatable deposition velocities.

Based on these previous discussion points a more detailed subregional approach can be taken to improve upon EPA's macro scale approach although an alternative scenario is proposed later. Table 2 shows alternative deposition flux rates for 4 categories of land use for which data is available in the literature. These data can then be applied to the 6 standard land use categories for the continental U.S. See Table 3.

The range of the stratified estimates which have some semblance of logic relative to sources and receptors across the U.S. is much more in alignment with EPA's current emissions inventory of known sources, i.e., 9,100 gm TEQ/yr. Although this number may be at the approximate level, the individual sources are given incorrect contributions by EPA. There are also several other well recognized sources which EPA did not inventory, e.g., sintering plants, secondary aluminum smelting, non-highway mobile sources, etc.

The zero deposition flux rate assigned as the lower limit for the Federal, and Rural range land use categories is because most of these areas are free of any significant upwind human activity as previously discussed. Obviously some very low ambient levels probably exist and low end deposition cannot be estimated. This may also be true of some portion of the Rural Forest category because there are private timberlands in the more remote areas in the western half of the continent. This excludes the potential intermittent and localized contribution from forest fires.

The available deposition data strongly suggests that long range transport may not be a significant mechanism of widespread agricultural crop contamination as EPA suggests. The Hites (1991) report to EPA is their only citation of evidence that long range transport of combustion related emissions is taking place. It should be noted there that there is an inconsistency between what Czuczwa and Hites (1986) and what Hites (1991) reported as the fate and transport mechanism. In the earlier citation the authors claim a high correlation between the congener profiles of the ambient data they used, i.e., Washington, D.C. and St. Louis and the Siskiwit Lake sediments. They further state that finding dioxins in the Siskiwit sediments "has made PCDD and PCDF ubiquitous in the environment." In the 1991 report a different set of ambient data were presented including that measured by the author et al. These data however did not show the good air and sediment congener profile correlations previously reported. The possible role of photodegradation was introduced to explain the shift in the congener distributions between sources and sinks. Most ambient data except those data from the vicinity of known point sources does not exhibit the congener profiles presented in the latter Hites report. In fact, most U.S. urban profiles look like the Washington, D.C. and St. Louis data.

We believe that there is a more logical and compelling explanation for the levels and congener profiles found in Siskiwit Lake. It is not a remote lake by any stretch of the imagination when potential nearby sources are considered, i.e., the Thunder Bay industry mix and commercial shipping. The commercial shipping in and out of Thunder Bay in 1983 involved some 1350 ships carrying 23.5

million metric tons of cargo from Thunder Bay most of which passed within 1-5 miles of the Isle Royale coastline. Although there have been no direct measurements of dioxins/furans from commercial vessel stacks there is no reason to believe that they would not be similar to those associated with diesel truck engines both in emission rates (ng/gal) and congener profiles. See Jones (1993) for a detailed discussion.

A major shift in ship and power technology took place after 1970 when steam turbine engines were replaced with diesel powerplants and Great Lakes ships became bigger and more fuel efficient. A historical fuel consumption profile in gal/mi. for the shipping past Isle Royale versus Hites' sediment data was estimated and is shown in Figure 1. The annual number of ships is also shown. This latter indicator does not reflect the change in ton mile fuel economy over the transition period just discussed. There has not been any other explanation which fits the sediment pattern as well as the proximate ship fuel consumption pattern. The change over to unleaded gasoline in 1975 and beyond has been suggested. However, the relative contribution of either leaded or unleaded gasoline powered vehicle dioxin emissions is insignificant in comparison to diesel powered vehicles and hence would not have caused such a major downward shift. The advent of air pollution control on incinerator sources is not consistent with the sediment pattern with respect to time. Further, it is unlikely that municipal incinerators, being relatively few in number, could influence Siskiwit Lake's sedimentation.

Smith et al. observed the same peaking and decline in sediment dioxin levels in Green Lake which is some 15 km east of Syracuse, New York. This lake is in a rural setting. However, it turns out that there are three major mobile sources which could influence the dioxin deposition in the lake as well as possibly explain the trend. Two of the three line sources are within 7 km and one of 16 km of Green Lake. They are:

The Erie Canal through Oneida Lake, the New York Throughway and the Conrail tracks (ex Penn Central). Although much of the historical multi-mode traffic data was not readily available, the trend in transport tonnage on the Erie Canal from 1950 onward and the train fuel use from 1973 on were available. Throughway traffic data for 1988 and 1993 were used to extrapolate back to 1960. These data plus a composite emissions factor trend are overlaid on the sediment trend data in Figure 2. There is an apparent correlation between the decrease in the emissions and sediment dioxin levels.

CONCLUSIONS

The direct answers to the three premise questions are as follows based on our critical review of EPA's documentation and other information we have gathered and synthesized.

Question 1: Are EPA's deposition estimates accurate based on the scientific evidence at hand?

Answer: No. EPA has grossly overestimated the total deposition in the U.S. Because they (a) did not interpret the available literature properly, (b) did not extrapolate European data to the U.S. case with necessary adjustments, and (c) did not double check their results by employing simple mass balance analyses. If a macro scale deposition model approach was an acceptable approach in the U.S. case and the best estimate

subregional deposition factors were used, the annual emissions would probably fall in the range of 4,700 - 12,400 gm TEQ/yr. These estimates more than likely will encompass the inventory of known sources once EPA corrects the errors in their existing inventory and adds additional sources which have been well documented in Europe. For example, EPA's inventory of hospital waste incinerator emissions is high by a factor of 35 while their mobile source inventory is low by a factor of at least 20.

Question 2: Are the deposition rates in the U.S. on the average higher or lower than in European countries?

Answer: Much lower. The spacial compression between industrial, suburban and rural areas in Europe is a greater than most of the continental U.S. There are many subregions of the U.S. which have no associated upwind center of human activity which is primarily responsible for dioxin emissions and their subsequent transport into rural or remote areas. Most of European countries experience 1 - 10 ng TEQ/m^2 /yr. of average deposition while in the continental U.S. the range is calculated to be between 0.6 and 1.6 ng/TEQ/m^2/yr. It is quite likely that remote background areas experience practically zero deposition flux. The EPA citation of Hites' conclusion that Siskiwit Lake represents a remote area is flawed because of obvious more local emissions sources, i.e., industry and shipping. An alternative deposition hypothesis is offered which does not incorporate long range transport as the principal mechanism of agricultural crop exposure in the U.S. Highly localized impacts due to line sources of mobile dioxin emissions in the form of farm machinery, transport trucks, trains, and highway traffic all represent equally plausible sources of crop exposure. The ambient air quality gradients do not exist across the major agricultural regions of the U.S. to support EPA's hypothesis.

Question 3: Does recirculation play a probable role in the fate and effects of current dioxin emissions?

Answer: Probably not. The closure between the anticipated inventory of known dioxin emission sources and the best estimate range of total emissions based on deposition flux analyses is the most compelling counter argument.

TABLE 1

DEPOSITION RATES CITED BY EPA

CITATION	DEPOSITION RATES ($ng/m^2/yr$)	EPA COMMENT/ASSUMPTIONS
1. Koester & Hites (1992)	370 - 540 Total PCDD/PCDF 1 - 2 TEQ	Perfect isomeric distribution
2. Smith et al. (1993)	375 Total PCDD/PCDF	Dep. rate for 86 - 90
3. Anderson et al. (1992)	1 TEQ	Snow in N. Sweden
4. Fernandez et al. (1992)	13 TEQ (nd = 0) 17 TEQ (nd = 1/2 d.l.)	1 mo. urban/sub. setting
5. Van Jaarsveld and Schutter (1992)	1 - 10 TEQ	Long range modeling of N. Europe
6. Hiester et al. (1993)	Urban 246 - 1687 Total PCDD/PCDF 3.6 - 30.3 TEQ Rural 420 Total PCDD/PCDF 4.4 TEQ	92 measurements nd's = 0
7. Liebl et al. (1993)	7.6 TEQ (ind/suburb) 1.5 TEQ (rural/ind) 1.1 TEQ (rural background)	11 mos. in 1992
8. Fiedler (1993)	1.8 - 7.3 TEQ (4.4 ave.) 7.3 - 36 TEQ 1,000 TEQ	Rural areas Ind. areas Few areas
9. Bowman et al. (1991)	38 Total PCDD/PCDF	Remote coastal, Sweden
10. Naf et al. (1992)	240 - 1,200 PCDD/PCDF 3 - 14 TEQ	Bothnian and Baltic Sea sediments

TABLE 2

BEST ESTIMATE DEPOSITION FLUX RATES

LAND USE	AUTHORS	TEQ FLUX ($ng/m^2/yr$)	COMMENTS/ASSUMPTION
Remote/Rural	Van Jaarsveld & Schutter	0.25	1/2 of modeled < .5 value
	Liebl/Boos	0.27	1/30 of Frankfurt 1992 dep. rate
			1/30 is urban/remote ratio from Boos[1]
Rural	Kühn & Steeg	0.9	9 - 18 km from Hamburg
	Liebl	2.45	
	Smith	1.09	Sediment data
Urban/Suburban	Liebl	7.7	1992 Frankfurt
	Kühn & Steeg	4.45	0 - 2 km from Hamburg
General	Van Jaarsveld & Schutter	11 (Belgium)	Average fluxes by country across Europe
		1.1 (Denmark)	
		3.8 (FRG)	
		8.2 (Netherlands)	
		2.4 (U.K.)	
		5.3 Average	

[1] Remote n.d. correction = average of all other data corrections.

TABLE 3

ESTIMATED DIOXIN T.E. DEPOSITION RATES BY LAND USE AND REGIONAL CHARACTERIZATION

REGIONAL LAND USE CHARACTERIZATION	AREA (10^6 AC)	DEPOSITION ($ng/m^2/yr$)	RATES ($gm/ac/yr$)	TOTAL DEPOSITION (gm/yr)
Developed	77.3	4.4 - 7.7	$17.8 - 31.2 \times 10^{-6}$	1376 - 2412
Federal	404.1	0 - .25	$0 - 1.0 \times 10^{-6}$	0 - 404
Rural Crop	422.4	0.9 - 2.45	$3.6 - 9.9 \times 10^{-6}$	1521 - 4182
Rural Pasture	129.0	0.9 - 2.45	$3.6 - 9.9 \times 10^{-6}$	464 - 1277
Rural Range	401.7	0 - .25	$0 - 1.0 \times 10^{-6}$	0 - 402
Rural Forest	373.9	0.9 - 2.45	$3.6 - 9.9 \times 10^{-6}$	1346 - 3702
Totals	1,933			4707 - 12,379
U.S. EPA Total	1,933	2 - 6	$8.1 - 24.3 \times 10^{-6}$	15,658 - 46,972

Zephyr Consulting

FIGURE 1

TRENDS IN THUNDER BAY MARITIME SHIPPING DATA & SISKIWIT LAKE SEDIMENT DIOXIN DEPOSITION RATES

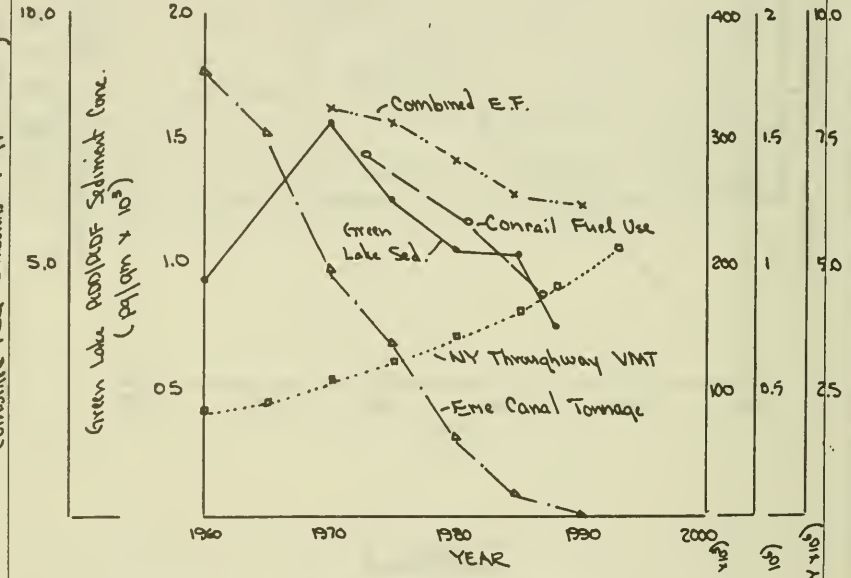

FIGURE 2

TRENDS IN VARIOUS MOBILE SOURCE FACTORS & GREEN LAKE SEDIMENT DIOXIN LEVELS

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

December 12, 1995

OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

Honorable Dana Rohrabacher
House of Representatives
Washington, D.C. 20515

Dear Congressman Rohrabacher:

I am professor of epidemiology at the School of Public Health at the John Hopkins University in Baltimore, MD. I also serve as Chair of the Executive Committee of the Science Advisory Board (SAB) at the Environmental Protection Agency (EPA). The SAB was established by Congress nearly two decades ago to provide independent, objective scientific evaluation of the technical foundations of the EPA's positions on issues. I have been a member of the Board for 6 years and Chair of its Executive Committee for over two years.

In that capacity I am submitting the following comments (which are adapted from the Executive Committee's letter transmitting the Board's report on dioxin) for your consideration and request their inclusion in the record of your hearing on the EPA's scientific reassessment of the risks associated with exposure to dioxin.

In 1988, EPA released two documents addressing risks from dioxins (*A Cancer Risk-specific Dose Estimate for 2,3,7,8-TCDD,* and *Estimating Exposure to 2,3,7,8-TCDD*) and requested that the SAB review them. The SAB report (SAB, 1989), released in November 1989, although not agreeing with several of the conclusions in the two documents, concluded that "both documents were carefully constructed and well written." The SAB report concluded with a recommendation to "...follow up on this excellent start..." by developing and validating new models for human exposure and for cancer and non-cancer risk endpoints, and to pursue active research programs, resolve questions and incorporate new data. The Agency initiated a significant effort addressing dioxin exposure and risk, and on September 13, 1994, released for public review and comment (59 FR 46980) a 2,400 page draft reassessment of the toxicity of, and human exposure to dioxin.

In December, 1994, the EPA Office of Research and Development (ORD) requested that the SAB review the reassessment document, and submitted a draft Charge addressing some 40 issues. The SAB Executive Committee approved the creation of an *ad hoc* Dioxin Reassessment Review Committee (DRRC) and appointed Drs. Morton Lippmann and Joan Daisey as Co-Chairs. The DRRC was developed by building on the SAB's Environmental Health and Indoor Air Quality/Total Human Exposure Committees, and adding (following an extensive review and recruitment process) additional Consultants to fill gaps in needed expertise and to add depth in key scientific areas. In addition to the Co-Chairs, 37 scientists were appointed to the Dioxin Reassessment Review Committee, including Dr. Michael Gough (as a Federal Expert), who is scheduled to testify before your Committee.

A final Charge for the review, encompassing 43 specific questions was adopted after discussions involving ORD and SAB staff, and the Co-Chairs (the detailed Charge is provided in section 2.2 of the enclosed report). The DRRC subsequently met on May 15-16, 1995, in Herndon, Virginia to hear briefings by EPA staff, to receive comments by members of the public, and to discuss the relevant issues of the Charge. Following the public meeting, the Committee's report was developed through a series of mail reviews of successive drafts. The final report was approved by the SAB Executive Committee at its public meeting on September 21, 1995. The only Members of the Dioxin Panel who participated in this meeting of the SAB Executive Committee were the Co-Chairs, Dr. Lippmann and Dr. Daisey. Admiral Elmo Zumwalt, who is scheduled to testify at your hearing, provided public comments at the Executive Committee meeting.

The enclosed report provides a detailed discussion of each of the specific issues raised by the Charge, and addresses some additional related questions which arose during the course of the review. The following comments provide a synthesis and overall perspective on the Committee's findings.

First, vis-a-vis the Exposure Assessment draft document, the Committee wishes to commend those responsible for doing a very credible and thorough job of assembling, integrating, and analyzing a very large body of data on dioxin source emissions, environmental levels, exposures, and human body burdens, all within the framework of human exposure assessment. The detailed recommendations of the DRRC largely address refinements, corrections and clarifications to the draft Exposure Assessment document, not substantive revisions.

The exposure reassessment identifies the major known sources of dioxins and provides a reasonable estimate of total emissions. The Committee recommends that new information on emissions from the incineration of medical waste (and other sources) be incorporated if appropriate, and that the estimates of uncertainties in the emissions inventory be improved for several emissions categories. The Committee also recommends adding an explicit statement to the final document noting that the fractional contributions of various types of emissions sources to total emissions cannot be assumed to be identical to the fractional contributions of those sources to human exposures. The Committee agrees with the EPA position that current levels of dioxin-like compounds in the environment derive primarily from anthropogenic sources and, based on available data, that the air-to-plant-to-animal pathway is most probably the primary way in which the food chain is impacted and humans are exposed. EPA should, however, take note of other potentially important exposure pathways, e.g., point source-to-water/sediments-to-fish and cigarette smoking. There is also a very large gap in our understanding of the potential atmospheric transformation of vapor-phase dioxin-like compounds and of the air-to-plant transfer coefficients of these compounds.

The document's estimate of average dioxin exposure is reasonable, but has substantial uncertainties because of limited data; it thus cannot provide an estimate of the complete distribution of exposures for the U.S. population. The Committee recommends that these points be noted clearly and explicitly in the Summary volume for the benefit of policy makers and the public. The Committee commends and fully supports EPA's on-going efforts to develop better data on concentrations of dioxins in food and in human tissue and regards these as very high priority research needs.

The Committee supports EPA's use of Toxic Equivalencies (TEQ) for exposure analysis, but also recommends that EPA carefully review the draft Exposure Assessment document and ensure that the congener-specific data are used in all instances (such as transport, transformation, and deposition processes) in which differences in the physical and chemical properties of the congeners are likely to be important.

The Health Assessment draft document, in its first seven (of nine) chapters, provides a comprehensive review of the scientific literature on the biological mechanisms involved in the uptake of dioxin and related compounds, the binding of these agents to receptor sites, their metabolism and retention in tissues, and the biological response at the cellular, organ, organ system, and

whole body levels. The Committee commends the EPA staff for this considerable accomplishment, and has made a number of comments and suggestions for relatively minor changes that should sharpen and clarify the content of the initial seven chapters. The Committee's most significant recommendations concerning these seven chapters center on the Agency's use of Toxic Equivalency Factors (TEF) to address the a broad range of dioxin-like compounds having the common property of binding to the Ah receptor, and producing related responses in cells and whole animals. The use of the TEFs as a basis for developing an overall index of public health risk is clearly justifiable, but its practical application depends on the reliability of the TEFs and the availability of representative and reliable exposure data. The Committee calls for clarifications in the specifications for TEFs of the various dioxin-like compounds for various health outcomes of concern, including the development of separate TEFs for the major compound classes, i.e., 2,3,7,8-TCDD, other dibenzodioxins and furans, and coplanar PCBs. The Committee is confident that final versions of Chapters One through Seven will not need further review by the SAB.

Chapter Eight, on modeling, must integrate both human and laboratory animal data, and is critical to the reassessment's overall success. The human data typically derives from accidents and industrial exposures, and are subject to many confounding factors. Animal studies often involve high-to low-dose extrapolations as well as cross-species extrapolation. Both types of such data are inadequate, by themselves, for estimating the human health risks of chronic, low-dose environmental exposures to dioxin and related compounds. Although this chapter reflects a great deal of effort, several Members of the Committee found the exposition of important points to be unclear. Chapter Eight is also weakened by its reliance on the standard EPA default assumption of a linear non-threshold model for carcinogenic risk. The Committee suggests that EPA consider, in future revisions, alternative models, allowing for minimal response at low environmental levels of exposure, which would be consistent with the body of available physiological, epidemiological, and bioassay data, as well as the recent information from pharmacokinetic modeling.

Almost all the Members of the Committee concur with EPA's judgment that dioxin, under some conditions of exposure, is likely to increase human cancer incidence. The conclusion with respect to dioxin-like compounds is less firm. In the case of dioxin, virtually all of the Committee believes that the animal studies would be categorized as "sufficient" and the studies of humans as "limited," providing for an overall categorization of

B_1, which would be expressed verbally as "Probably Carcinogenic to humans with limited supporting information from human studies." The Committee (on the basis of similar effects) would support the same designation for dioxin-like materials. PBBs and PCBs would receive ratings of B_1 and B_2, respectively.

Chapter Nine, on risk assessment, was not as thoroughly peer-reviewed before submission to the SAB as were the earlier chapters, and needs to be revised considerably to reflect the changes being made in Chapters 1-8 and to deal with the areas of weakness discussed below. The revised chapter would greatly benefit from an external peer review by an appropriate group. More specifically, the Committee identified, and wishes to emphasize to the Agency, particular areas of both strength and weakness in Chapter 9.

Three major strengths are apparent. First, by focusing serious attention on various non-cancer effects (both human health and ecological effects), the Agency has dispelled any mis-impression that EPA's risk assessment process is overly preoccupied with carcinogenic effects. Second, by evaluating an entire class of compounds, rather than a single compound, the Agency has responded to criticism that its risk assessment process can only address issues on a chemical-by-chemical basis. Third, a useful comparative perspective is provided in the draft conclusions where the Agency highlights the fact that the margin of safety (between background exposures and levels of exposure where effects have been observed in test animals) for dioxin-like compounds is smaller than the EPA usually sees for many other compounds.

Three major weaknesses were also noted. First, the presentation of scientific findings portrayed in the draft document's conclusions is not balanced *vis-a-vis* the possible risks posed by exposure to dioxin, with a tendency to overstate the possibility for danger. Second, important uncertainties associated with the Agency's conclusions are not fully identified and subjected to feasible analyses. Finally, the characterization of non-cancer risk is not performed in a manner which can facilitate meaningful analysis of the incremental benefits of risk management alternatives.

This letter can only highlight the major points of a detailed and extensive review by 39 SAB Members and Consultants of a 2000+ page document. Perforce, the letter cannot convey the many lesser, but important, findings and suggestions in the Committee's report. Also, it is important to note that although there is a broad consensus on most issues, not every

Member/Consultant on the Committee agreed fully with every finding, which is not surprisingly given the multiplicity and complexity of the issues and the balanced range of views incorporated in the Panel. Specific instances are noted in the report itself.

I hope that the information provided above will be of value to your Subcommittee in its deliberations.

Sincerely,

Genevieve M. Matanoski

Dr. Genevieve Matanoski, Chair
Science Advisory Board

Enclosure

E. R. ZUMWALT, JR.
ADMIRAL, U. S. NAVY (RET.)

December 29, 1995

The Honorable Dana Rohrabacher
Chairman, Subcommittee on Energy and Environment
U.S. House of Representatives Committee on Science
2320 Rayburn House Office Building
Washington, DC 20515-6301

Dear Mr. Chairman:

Attached are the documents from which I was reading during the committee hearings on *Scientific Integrity and Federal Policies and Mandates: Case Study 3--EPA's Dioxin Reassessment* held on Wednesday, December 13, 1995, which Congressman George Brown requested that I provide for printing in the record.

Thank you for your gracious comments to me.

Sincerely,

E. R. Zumwalt, Jr.

E. R. Zumwalt, Jr.
Admiral, USN (Ret.)
Chairman, Agent Orange Coordinating Council

1000 Wilson Boulevard, Suite 3105
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Fax: (703) 528-5795

Enclosure

cc w/enc: The Honorable George E. Brown, Jr.

GREENPEACE

12/12/95

TO: Admiral Elmo Zumwalt
FROM: Rick Hind
RE: Dioxin Hearing at Science subcommittee

The following information may be of use to you when you testify tomorrow before Representative Rhohrabacher's subcommittee hearing on EPA's dioxin reassessment.

As you know, although we nominated 7 expert witnesses to testify, Mr. Rhohrabacher's hearing witness list you are the only one of these witnesses that will be allowed to testify. As a result, you are the only hearing witness representing non-governmental, non-industry interests. The other two non-governmental witnesses have consistently testified in favor of the regulated industry. They are Dr. Michael Gough and Dr. Kay Jones (some examples of their activities are described below.)

In addition, I have attached two recently peer reviewed articles. The first is an article published in the September, 1995 issue of Environmental Health Perspectives by Michael J. Devito, Linda S. Birnbaum, William H. Farland and Thomas A Gasiewicz. In sum, this article is a peer reviewed version of Chapter 9 of EPA's dioxin reassessment. It's bottom line conclusion is: "Available human data suggest that some individuals may respond to dioxin exposures with cancer and noncancer effects at body burdens within one to two orders of magnitude of those in the general population."

The second article was a study of 1,189 chemical workers in Hamburg, Germany published December 1, 1995 in the Johns Hopkins American Journal of Epidemiology by Dieter Flesch-Janys, Jurgen Berger, Petra Bum, Alfred Manz, Sibylle Nagel, Hiltraud Waltsgott and James H. Dwyer. Again, the bottom line conclusion is: "These findings indicate a strong dose-dependent relation between mortality due to cancer or ischemic heart diseases and exposure to polychlorinated dioxins and furans."

Dr. Michael Gough is a consultant, formerly with the Office of Technology Assessment (OTA). Earlier this year while at OTA Gough told the Los Angeles Times, "EPA played very fast and loose with it own rules in order to come to the conclusion that (secondhand) smoke is a carcinogen."

In 1990 while working for the Industry Task Force II on 2,2-D (an herbicide) Gough disputed National Cancer Institute studies that showed an 8-fold increased risk of cancer to farmers using 2,4-D.

In 1988 Gough while working for Resources for the Future (which is funded in part by Dow Chemical, Dupont, Monsanto and the

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Chemical Manufacturers Association) disputed the way in which EPA made its estimate of cancer risk for dioxin.

In 1987, Gough also authored a report for the paper industry's research arm, the National Council on Air and Stream Improvement (NCASI) entitled "Executive Summary -- Dioxin: A Critical Review of its Distribution, Mechanism of Action, Impact on Human Health, and Setting of Acceptable Limits."

Also in the mid 1980s Gough worked with the consulting firm ENVIRON which was doing risk assessments in support of garbage incinerators proposals. ENVIRON is now the lead consultant for the American Forest & Paper Association efforts to challenge the EPA's reassessment of dioxin.

Dr. Kay Jones is a frequent critic of EPA's air pollution program. He currently works for the Seattle based Zephyr Consulting firm on behalf of the incinerator industry.

In 1989 while working for R.F. Weston, Jones urged the City of Detroit, Michigan to begin operating the world's largest trash incinerator WITHOUT adequate air pollution control systems. In 1990, stack tests proved the need for such a system to reduce mercury emissions. The error cost Detroit millions in tax dollars.

Jones also has insisted that dioxin emissions from diesel powered trucks and buses is greater than dioxin emissions from incinerators, contrary to the largest identified source of dioxin according to the EPA.

In addition to the information on these industry witnesses, I have attached a segment of a recent report we did on Dow chemical regarding Dow's efforts to influence science and policy on dioxin. In particular, this report documents the chemical and paper industry support of work by Dr. Greenlee and Dr. Graham. Greenlee and Graham were also on the recent EPA Science Advisory Board panel that review the dioxin reassessment and were given lead responsibility for writing the critique of Chapter 9 of the reassessment. As a result, their criticisms did NOT reflect the consensus of the SAB panel as noted by dissenting members.

Comparisons of Estimated Human Body Burdens of Dioxinlike Chemicals and TCDD Body Burdens in Experimentally Exposed Animals

Michael J. DeVito,[1] Linda S. Birnbaum,[1] William H. Farland,[2] and Thomas A. Gasiewicz[3]

[1]Health Effects Research Laboratory, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711 USA; [2]Office of Health and Environmental Assessment, U.S. Environmental Protection Agency, Washington, DC 20460 USA; [3]Department of Environmental Medicine, University Rochester School of Medicine, Rochester, NY 14642 USA

Humans are exposed to mixtures of polyhalogenated aromatic hydrocarbons, and the potential health effects of these exposures are uncertain. A subset of this class of compounds produce similar spectra of toxicity in experimental animals as does 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), and these chemicals have been classified as "dioxins." In this study, we compared the body burdens of dioxins that produce effects in experimental animals to body burdens associated with these effects in humans. Human body burdens were estimated from lipid-adjusted serum concentrations of dioxins, assuming dioxins are equally distributed in body fat and an adult has 22% body fat. The toxic equivalency factor (TEF) method was used to calculate body burdens of dioxins in humans. These calculations included dibenzo-*p*-dioxins, dibenzofurans, and polychlorinated biphenyls. In the general population, average background concentrations were estimated at 58 ng TCDD equivalents (TEQ)/kg serum lipid, corresponding to a body burden of 13 ng TEQ/kg body weight. Populations with known exposure to dioxins have body burdens of 96–7,000 ng TEQ/kg body weight. For effects that have been clearly associated with dioxins, such as chloracne and induction of CYP1A1, humans and animals respond at similar body burdens. Induction of cancer in animals occurs at body burdens of 944–137,000 ng TCDD/kg body weight, while noncancer effects in animals occur at body burdens of 10–12,500 ng/kg. Available human data suggest that some individuals may respond to dioxin exposures with cancer and noncancer effects at body burdens within one to two orders of magnitude of those in the general population. *Key words:* dioxins, polychlorinated biphenyls, risk assessment, toxic equivalency factors. *Environ Health Perspect* 103:820–831 (1995)

Over the last 30 years, an abundance of studies have clearly demonstrated that 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) is extremely toxic to experimental animals (*1–3*). Fish and wildlife are also sensitive to the toxic effects of this chemical (*4*). TCDD is carcinogenic in male and female rats and mice, male hamsters, and male and female fish (*5,6*). Reproductive and developmental toxicity has been observed in all experimental animals tested. Immunotoxic effects occur in mice, rats, and nonhuman primates exposed to low doses of TCDD (*7*). Evidence to date indicates that the actions of TCDD are mediated by the Ah receptor (*8,9*) which functions as a signal transducer and transcription factor. In many ways the actions of the Ah receptor are similar to those of the steroid hormone receptors (*10,11*), although the Ah receptor is not a member of this superfamily of proteins (*12,13*). Other halogenated dibenzo-*p*-dioxins and dibenzofurans substituted in all four lateral positions also have high binding affinity to the Ah receptor and induce the same spectrum of toxicity as TCDD (*14*). In addition, certain polyhalogenated biphenyls, naphthalenes, and diphenyl ethers are Ah receptor agonists. Humans are exposed to complex mixtures of these chemicals; estimates of daily exposure to TCDD or "dioxinlike" (all 2,3,7,8-halogenated dibenzo-*p*-dioxins and dibenzofurans as well as the dioxinlike polychlorinated biphenyls) chemicals is 3–6 pg TCDD equivalents/kg/day in the United States (*15,16*). The subclass of the polyhalogenated aromatic hydrocarbons with dioxinlike activity are referred to as dioxins in this article.

Although the toxic effects of dioxins in experimental animals are unequivocal, their toxic effects in humans are less certain. Chloracne is the only toxic effect induced by dioxins for which there is unequivocal evidence linking exposure to effect in humans (*17*). The uncertainty of other toxic effects of dioxins in humans is due to the scarcity of human populations with high dose exposures, limited data on the body burdens of dioxins present in these populations, the difficulty in assessing sensitive toxic endpoints in humans, and the lack of knowledge about likely, but unknown, genetic factors that may influence the relative susceptibility of individuals. Dioxins produce some of the same biochemical alterations in humans and experimental animals (*18*). Several recent epidemiological studies suggest an association between dioxin exposure and increased incidence of cancer (*19–23*) and increased incidence of altered glucose tolerance in exposed populations (*24,25*). One way to determine the strength of an association between dioxin exposure and a toxic effect in humans would be to compare the dose of dioxin that is required to produce an effect in animals to the dose of dioxin in humans that is associated with a similar toxic effect. While it is clear that for some toxic effects, such as lethality and body weight loss, there are marked species differences in susceptibility to dioxins, many recent studies have also noted that for other endpoints, such as reproductive and developmental effects, most animal species respond at similar doses (*9,26*). Thus, the dose of dioxin that produces a particular effect in experimental animals might be expected to be similar to the dose of dioxin associated with that same effect in humans.

Although the hypothesis that toxic doses of dioxins in animals and humans are similar for most responses is theoretically testable using data from accidentally exposed human populations, there are some difficulties. In particular, it is often difficult to determine the human dosage at the time of exposure. In experimental studies, animals are administered a known amount of dioxin and evaluated at a specific time after the treatment. In humans the actual exposure is unknown and often difficult to estimate. Several epidemiological studies determined serum concentration of dioxins in exposed and control populations (*19–25*). Although the dose to the individuals in these studies is uncertain, the body burdens of dioxins in these populations can be estimated at a specific point in time. In addition, serum and tissue dioxin concentrations from populations in the United States with-

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out any unusually high exposures have been reported from several different laboratories (*27–30*). All humans in industrialized countries are presumed to carry a body burden of dioxins based primarily on consumption of minute quantities of dioxin in the food supply. Here we compare the body burdens of dioxins that produce effects in experimental animals to the body burdens associated with effects in humans, based on the clinical findings observed during epidemiological studies. A comparison of the *in vitro* effects of dioxins on human and animal tissues and cell cultures is also presented. This analysis suggests that some of the effects observed in experimental animals also occur in humans and that the body burdens of dioxins associated with these effects (adaptive and/or toxic) are similar between animals and humans.

Methods

Comparisons of animal and human tissues or cell lines studied under *in vitro* conditions are shown in Table 1. This list is not meant to be exhaustive. The data presented are from peer-reviewed literature and include only those papers that compared animal and human tissues in the same study or laboratory.

We estimated human body burdens based on analyses of dioxin in serum or tissue in the cited literature. Several assumptions were used to derive body burdens from these values. Dioxins are assumed to be equally distributed in the body lipid with all tissues having the same concentration of TCDD when expressed on a lipid-adjusted basis (*31–33*). Thus, serum levels presented as lipid-adjusted are assumed to be equivalent to adipose tissue levels expressed as lipid-adjusted values. In addition, we assumed that for the average person, 22% of the body weight is lipid or fat (*34*). To estimate body burdens in humans, lipid-adjusted serum or adipose tissue concentrations (expressed as ng TCDD/kg or TEQ/kg) were multiplied by 0.22 (*34*), the fraction of body weight that is fat.

Some of the body burden estimates in humans presented here are based on tissue concentrations of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin alone. In all cases, humans were likely to have been exposed to many dioxinlike chemicals that bind to the Ah receptor and produce the same spectrum of toxic effects in experimental animals as TCDD (*2,14,26*). To account for exposure to additional dioxins, the toxic equivalency factor method (TEF) was used (*14,35–38*). TEFs are relative potency factors used to convert the amount of dioxins in a sample to TCDD equivalents or TEQs (*14,35–38*). TEFs were assigned only to 2,3,7,8-chlorine substituted dibenzo-*p*-dioxins and dibenzofurans, the coplanar polychlorinated biphenyl(s) (PCBs) (IUPAC nos. 77, 81, 126, and 169) and the mono-*ortho*-substituted PCBs (IUPAC nos. 105, 114, 118, 156, 157, 167, and 189). The TEF values used for the dibenzo-*p*-dioxins and dibenzofurans were the U.S. EPA interim TEF values, which represent an internationally accepted convention for assessment of dioxins (*37,38*). The TEF values used for the dioxinlike PCBs were the World Health Organization values, which resulted from a recent international meeting of dioxin and PCB experts (*38*). Hence, body burdens for this complex mixture of related chemicals are expressed in terms of TEQs.

Body burden estimates in populations exposed to background levels of dioxins were based on published studies that measured serum concentrations of 2,3,7,8-chlorine substituted dibenzo-*p*-dioxins (CDDs) and dibenzofurans (CDFs) and dioxinlike PCBs in populations with no unusually high exposure to dioxins (*27–30,39*). Serum concentrations of CDDs and CDFs have been measured in a number of different populations from several studies. Schecter (*27*) presented data indicating that the average whole-blood CDD/CDF concentration in U.S. (n = 100) and German (n = 85) populations were similar when presented on a TEQ basis (41 and 42 ng TEQ/kg whole blood, lipid adjusted). More extensive studies of U.S. populations indicate that the national average for serum CDD/CDF concentrations is 28 ng TEQ/kg serum lipid (*39*). Much smaller studies of congener-specific PCB serum or adipose tissue concentrations have been published that indicate that average dioxinlike PCB concentrations range from 8 to 17 ng TEQ/kg tissue lipid in U.S. populations (*28,30*). The range of average tissue TEQ concentrations for CDDs/CDFs is 28–41 ng TEQ/kg lipid and for the PCBs the range is 8–17 ng TEQ/kg lipid. Based on these studies, average background dioxin tissue concentrations range from 36–58 ng TEQ/kg lipid. In these populations, TCDD contributes approximately 12% of the total TEQ.

Body burden estimates in exposed populations were based on the published literature. These populations were assumed to have background exposures, in addition to the specific exposures determined in the study. The level of dioxins in exposed populations were often determined years after the initial exposure. Body burdens were estimated at the time of maximal exposure assuming the rate of total body elimination of dioxins is linear with respect to time and dose and a assuming 7.1-year half-life (*40*).

Determination of maximum body burdens in experimental animals was based on the administered dose and the rate of elimination of dioxin from the animal. Total body half-life of TCDD in experimental animals was assumed to be first order with respect to time and dose. In several cases, body burdens in animals were based on tissue levels determined in the study.

Effects seen in epidemiological studies have been divided into two categories. The first category (Table 2) is for effects that have been causally associated with exposure to dioxins. These are effects for which there is strong evidence that the responses observed are due to exposure to dioxins and/or related compounds. Typically, adverse effects with demonstrated causality

Table 1. Comparison of the effects of TCDD exposure on human and animal tissue *in vitro*

Effect	Species/tissue	Concentration (nM)	Reference	Appendix note[a]
TCDD binding to Ah receptor (K_d)	Mouse (C57Bl/6)	0.7	(*42*)	a
	Human	1.5	(*42*)	a
Induction of CYP1A1 (EC_{50})	Lymphocytes			
	Mouse	1.3	(*46*)	b
	Human	1.8	(*46*)	b
Cytotoxicity (LOEL)	Embryonic palate			
	Mouse	0.1	(*47*)	c
	Rat	100	(*47*)	c
	Human	100	(*47*)	c
Inhibition of proliferation (LOEL)	Thymocytes			
	Mouse	0.1	(*48*)	d
	Human	0.1	(*49*)	d
	Lymphocytes			
	Mouse	3.0	(*50*)	e
	Human	0.3	(*50*)	e
Inhibition of IgM secretion (LOEL)	Lymphocytes		(*50*)	e
	Mouse	3.0		
	Human	0.3	(*50*)	e

LOEL, lowest observed effect level.
[a]The data and methodology used to determine each value are presented in the appendix under the letter indicated.

Table 2. Responses in humans causally associated with exposure to dioxins and comparable effects in experimental animals

Effect	Species	Experimental dose	Body burden (ng/kg)	Reference	Appendix note[a]
Chloracne	Human		96–3,000	(51,52)	f
	Monkey	1,000 ng/kg	1,000	(53)	g
	Rabbit	4 ng/rabbit, 5 days/week/4 weeks	23	(54)	h
	Mouse	4,000 ng/kg, 3 days/week/2 weeks	13,900	(55)	i
Downregulation of EGFR (maximal effect)	Human (placenta)		2,130	(18,56)	j
	Rat (liver)	125 ng/kg/day, 30 weeks	2,582	(57)	k
	Mouse (liver)	10,000 ng/kg	10,000	(58)	l
Induction of CYP1A1 (maximal effect)	Human (placenta)		2,130	(18,56)	j
	Rat (liver)	125 ng/kg/day, 30 weeks	2,582	(59)	k
Induction of liver CYP1A1 (LOEL)	Rat	1 ng/kg	1	(60)	m
	Mouse	1.5 ng/kg/day, 5 days/week/13 weeks	23	(61)	n
Hepatic sequestration	Human		300	(62)	o
	Rat		100	(62)	o
Background	Human	TCDD	1.1		p
		PCDD/PCDF	6–9		p
		PCDD/PCDF/PCB	8–13		p
	Rat		1	(67)	q
	Mouse		4	(61)	r

Abbreviations: EGFR, epidermal growth factor receptor; LOEL, lowest observed effect level; TCDD, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin; PCDD, polychlorinated dibenzodioxin; PCDF, polychlorinated dibenzofuran; PCB, polychlorinated biphenyl.
[a]The data and methodology used to determine each value are presented in the appendix under the letter indicated.

are associated with high-level exposure and are severe enough to clearly indicate a relationship with such exposure. Chloracne is an example of such an adverse effect. In addition, biochemical changes such as induction of CYP1A1 and decreases in EGF receptor autophosphorylation are included in this category because there is significant experimental evidence that these effects occur through activation of the Ah receptor and are therefore causally related to exposure to dioxinlike chemicals.

A second category (Table 3) was assigned for effects associated with dioxin exposure for which a causal link has not been definitively proven. Effects included in this category are decreased birth weight, decreased growth, delayed developmental milestones, cancer, decreased testosterone levels, and increased risk of diabetes. In both Tables 2 and 3, body burdens in experimental animals are presented for comparable toxic effects to those seen in the epidemiological studies.

Table 4 presents body burdens in experimental animals that produce an effect for which no comparable human epidemiological data are yet available. The current epidemiological database consists primarily of studies on adult male populations; few studies of women or children are available. Only effects seen at low doses or body burdens in experimental animals were chosen for this table to estimate the low end of the animal effect range; effects such as thymic atrophy, the wasting syndrome, or death are not included. The specific assumptions and data used to derive each value presented in Tables 1–4 are presented in the appendix.

Results

Comparisons of the *in vitro* effects of TCDD on animal and human tissues or cell lines are shown in Table 1. A number of investigations have found the Ah receptor present in humans to have a similar but slightly lower binding affinity for TCDD than the Ah of many other species (*42–45*). The concentration of TCDD required to produce equivalent effects in animal and human tissues is not significantly different for responses as varied as induction of CYP1A1 in lymphocytes and thymocyte proliferation (Table 1). For several responses, the effective concentration of TCDD differs in animal and human tissue by an order of magnitude or greater. Cytotoxic effects induced by TCDD in organ cultures of developing palate occur at concentrations 1000 times lower in mouse tissue than in either human or rat tissue (*48*). Cultures of embryonic human and rat palatal shelves respond at the same concentrations (*49*). Inhibition of lymphocyte proliferation and secretion of IgM in mouse splenic lymphocytes requires 10 times the concentration of TCDD compared to human tonsilar lymphocytes (*50*).

Comparisons of body burdens associated with *in vivo* effects demonstrate similar correlations between animals and humans. Body burden estimates in individuals with chloracne vary by almost two orders of magnitude (Table 2). In subjects with chloracne, exposures resulted from either industrial or accidental poisonings. In experimental animals, species differences in body burdens of TCDD that induce chloracne vary by almost three orders of magnitude, with the rabbit the most sensitive and the hairless mouse the least sensitive. The range of body burdens that result in chloracne in humans (96–3,000 ng TEQ/kg body weight) and animals (23–13,900 ng TCDD/kg body weight) are similar. It should be noted that the first of these ranges represents interindividual variation while the second includes interspecies variation.

Body burdens in the general population were determined based on TCDD alone, total PCDDs/PCDFs, and total PCDDs/PCDFs/PCBs (Table 2). The average body burden of TCDD in the general population is approximately 1.1 ng TCDD/kg body weight. The average body burden in the general population for total PCDDs/PCDFs is 9 ng TEQ/kg body weight and for total PCDDs/PCDFs/PCBs is 13 ng TEQ/kg body weight.

Rice oil contaminated with PCDFs and PCBs, among other contaminants, was ingested by men and women from Taiwan (Yu-Cheng incident); these individuals have been carefully studied since the poisoning incident (*18,56,63–65*). Biochemical changes in placentas from the women exposed during the Yu-Cheng incident are similar to the biochemical changes in rodent liver from animals exposed to TCDD. Near maximal downregulation of human placental epidermal growth factor receptor autophosphorylation occurs at similar body burdens, as do comparable decreases in hepatic epidermal growth factor receptor in rats and mice (Table 2). Maximal induction of hepatic cytochrome P-450 1A1 (CYP1A1) in rats and mice by TCDD occurs at body burdens similar to those that elicit maximal increases of CYP1A1 in human placenta from the individuals exposed during the Yu-Cheng incident. The lowest observable effect level (LOEL) for enzyme induction in animals is 1 and 23 ng TCDD/kg body weight in rats (*60*) and

Table 3. Responses in humans associated with dioxin exposure and comparable effects in experimental animals

Effect	Species	Experimental dose	Body burden (ng/kg)	Reference	Appendix note[a]
Cancer	Human		109–7,000	(19,22)	s
	Hamster	100 µg/kg/month/ 6 months	137,000	(58)	t
	Rat	100 ng/kg/day, 2 years	2,976	(69)	u
	Mouse	71 ng/kg/day, 2 years	944	(70)	v
Tumor promotion	Rat (liver)	125 ng/kg/day, 30 weeks	2,582	(71)	k
	Mouse (skin)	7.5 ng/week, 20 weeks	830	(72)	v
Decreased birth weight	Human	Maternal body burden	2,130	(18,56)	j
	Rat	400 ng/kg, maternal dose	400	(73)	w
	Hamster	2,000 ng/kg, maternal dose	2,000	(8)	w
Decreased growth	Human	Maternal body burden	2,130	(63)	j
	Rat	1,000 ng/kg, maternal dose	1,000	(75)	w
Delayed developmental milestones	Human	Maternal body burden	2,130	(64,65)	j
Object learning	Monkey	0.151 ng/kg/day, Maternal body burden	42 ng/kg	(66)	x
Decreased testosterone	Human		44–122	(41)	y
	Rat	12,500 ng/kg	12,500	(76)	u
Altered glucose homeostasis	Human	-	99–140	(24,25)	z, aa
	Guinea pig	30 ng/kg	30	(78)	bb
	Rat	100 ng/kg/day, 30 days	2,000	(79)	u

[a]The data and methodology used to determine each value are presented in the appendix under the letter indicated.

Table 4. Low dose effects in animals exposed to dioxins

Effect	Species	Experimental dose	Body burden (ng/kg)	Reference	Appendix note[a]
Decreased offspring viability	Rhesus monkey	0.76 ng/kg/day, 4 years	345	(80)	x
	Rat	1,000 ng/kg	1,000	(74)	w
	Hamster	18,000 ng/kg	18,000	(81)	w
Altered lymphocyte subsets	Marmoset	0.3 ng/kg/week, 24 weeks and 1.5 ng/kg/week, 12 weeks	10	(82)	cc
		10 ng/kg	10	(83)	cc
Enhanced viral susceptibility	Mouse	10 ng/kg	10	(84)	dd
Endometriosis	Monkey	0.151 ng/kg/ day/4 years	69	(85)	x
Decreased sperm count	Rat	64 ng/kg, maternal dose	64	(59)	w
Testis abnormalities	Rat	12,500 ng/kg	12,500	(76)	u
	Mouse	100 µg/kg	100,000	(77)	ee

[a]The data and methodology used to determine each value are presented in the appendix under the letter indicated.

mice (61), respectively, which is within the range of background human body burdens of 13 ng TEQ/kg body weight.

Disposition of dioxins is dose dependent in animals and humans (62). The body burden necessary for hepatic sequestration is similar for rats and humans (62). In animals, the body burden of TCDD that produces a carcinogenic effect ranges from 944 ng TCDD/kg body weight in mice (70) to 137,000 ng TCDD/kg in hamsters (58) (Table 3). Body burdens in animals exposed to carcinogenic doses of TCDD are 73- to 10,500-fold greater than background human TEQ body burdens. In epidemiological studies that indicate an association between TCDD exposure and increased incidence of cancer, body burdens were estimated between 109 and 7,000 ng TCDD/kg at the time of highest human exposure. Background human TEQ body burdens are approximately 8–540 times less than human TEQ body burdens estimated from the studies that associated dioxin exposure with increased cancer incidence.

Decreased birth weights were reported in children born to women exposed during the Yu-Cheng incident (18,56). These women were highly exposed and had an average body burden of approximately 2,130 ng TEQ/kg body weight. Body burdens of dioxins in experimental animals that decrease birth weight range from 400 to 2,000 ng TCDD/kg body weight in rats and hamsters (73,74) (Table 3).

Children of the Yu-Cheng mothers are not only smaller at birth but remain smaller throughout childhood compared to children of unexposed women (63). In rats, pups of dams exposed to 1,000 ng TCDD/kg body weight not only have decreased birth weights but consistently weigh less than controls up to 63 days of age, though they do recover upon reaching sexual maturity (75).

The Yu-Cheng children also exhibit delayed developmental milestones (64,65). Behavioral effects after perinatal TCDD exposure have been observed in rhesus monkeys born to mothers exposed to approximately 5 ppt TCDD in the diet (66). Body burdens in the rhesus mothers were 42 ng TCDD/kg body weight, which is approximately 51 times less than the TEQ body burden in the Yu-Cheng women, but only 3.2 times higher than average TEQ body burden in the general population.

Although some of the responses seen in experimental animals appear to occur in humans at similar body burdens, there are significant differences in the body burden estimates for decreased testosterone levels (41) and between human and animals. Based on these limited data, if decreased testosterone in humans is due to dioxin toxicity, then some humans may be approximately 280 times more sensitive than are rats for dioxin-induced decreases in testosterone.

Increased incidence of diabetes in populations exposed to dioxins has been reported in two studies with body burdens ranging from 99 to 140 ng TEQ/kg. While TCDD-induced diabetes has not been studied in experimental animals, there are reports of altered glucose homeostasis. Alterations in glucose uptake in adipocytes isolated from guinea pigs treated with TCDD occurs at body burdens 3–4 times lower than human populations with increased incidence of diabetes and altered glucose tolerance (24,25). Decreased serum glucose in rats occurs at body burdens 14–20 times higher than the increased incidence of diabetes and altered glucose tolerance in humans.

Table 4 presents estimated body burdens of TCDD in experimental animals from studies that report low-dose effects for which no comparable human studies are available. LOELs for decreased offspring viability/fetal viability vary from 345 ng/kg in monkeys to 18,000 ng/kg in hamsters. Alterations in lymphocyte subsets in juvenile marmosets is 10 ng TCDD/kg body weight (*82,83*). Enhanced viral susceptibility, as measured by increased mortality, occurs in mice at body burdens of approximately 10 ng TCDD/kg (*84*), which is equivalent to the body burden seen in unexposed humans and approximately twice the level in untreated mice. Effects such as increased incidence of endometriosis in rhesus monkeys (*85*) and decreased sperm count in offspring of rats treated with TCDD (*74,86*) occur at body burdens approximately five times that of unexposed human populations.

Discussion

A number of investigators have found the Ah receptor present in human tissues to have a similar, but slightly lower, affinity for TCDD than those receptors present in many other species (*42–45*). For example, a recent study determined that the apparent binding affinity of TCDD to the Ah receptor ranged from 0.4 to 15 nM in 115 human placentas and from 1 nM in the TCDD responsive C57Bl/6J mouse to 16 nM in the TCDD nonresponsive DBA/2 mouse. The binding affinity of TCDD to the Ah receptor is similar in mice, rats, hamsters, guinea pigs, and monkeys (*87*), and there is no obvious correlation between TCDD binding affinity to the Ah receptor and species sensitivity to the lethal or toxic effects of TCDD (*87*). Thus, our knowledge of the quantitative relationship between binding affinity and interspecies responsiveness does not provide adequate information to determine whether humans are more or less responsive than other species based solely on the binding affinity of TCDD to the Ah receptor.

Comparisons of human tissues or cell lines with similar animal tissues or cell lines demonstrate that from relatively simple responses, such as enzyme induction to more complex phenomena, such as cytotoxicity and proliferation, human tissue responds in the same manner as animal tissue and at similar concentrations (Table 1). These *in vitro* studies suggest that humans will respond to dioxin and that some of these responses may be adverse.

The doses of dioxins that produce lethality in experimental animals can vary by more than three orders of magnitude: guinea pigs are the most sensitive and hamsters are the least sensitive (*1–3*). Because of this large variability in lethal effects, there has been an expectation that large species differences exist for all other effects. The data presented in the tables indicate that for a particular effect, some species may be extremely sensitive and some may be resistant, but many species respond at similar doses (i.e., within an order of magnitude). All experimental mammalian species examined respond to most of the adverse effects of dioxins at some dose. It is possible that humans may be resistant to some of the toxic effects of dioxins, but it seems highly unlikely, given the data currently available, that humans are refractory to all of the toxic effects of these chemicals.

Dioxins are unequivocally potent toxicants in experimental animals, yet the human health effects of exposure to these chemicals remain controversial. Comparisons of human and animal body burdens alone cannot prove a cause-and-effect relationship between toxicity and exposure in humans observed in an epidemiological study. However, this information can be used to increase or decrease our confidence that a particular adverse health effect observed in an epidemiological study was associated with the exposure to dioxins.

In addition, the present analysis required several assumptions in estimating both animal and human body burdens. These assumptions were required due to the lack of complete data on pharmacokinetics, toxic equivalency factors, species extrapolation, and, for humans, lack of information on daily dose or exposures. Hence, the information presented here can be used to direct research efforts to provide more accurate information on these topics.

There are some uncertainties associated with the assumptions used to estimate body burdens of dioxins in animals and humans. Unlike the experimental animal toxicology studies examined, humans are exposed to multiple chemicals. However, in the epidemiological studies, many of these chemicals interact with the Ah receptor as either agonists, partial agonists, or possibly antagonists. Assumptions of the relative potency of the chemicals and their distribution in the humans will result in uncertainties that are difficult to quantify given the present database. However, these uncertainties are likely well within an order of magnitude because body burdens of TCDD alone represent 10% of the total TEQ body burden due to all the PCDDs, PCDFs, and PCBs (Table 2).

Human body burdens are estimated using the TEF methodology. The TEF values derived by the U.S. EPA and the World Health Organization were based on scientific judgment as well as experimental data (*37,38*). In setting a TEF value, more weight was given to long-term, *in vivo* studies than to *in vitro* or acute *in vivo* studies (*14,36–38*). In fact, although wide ranges of TEF values have been reported for specific congeners, the variability is within a factor of 10 when the *in vivo* data are used to set the TEF value (*14,37,38*).

The TEF methodology assumes additivity of toxic potential. The use of the TEF methodology has been validated for complex mixtures of chlorinated dibenzo-*p*-dioxins for effects such as enzyme induction and tumor promotion (*88*). The interaction of mixtures containing both dioxin-like and non-dioxinlike chemicals has not been studied as thoroughly. There are reports of antagonistic (*89–91*) and synergistic (*92,93*) interactions of dioxins and non-dioxinlike PCBs. The demonstration of nonadditive interactions increases the uncertainty of these values. Finally, the TEF scheme includes only full agonists of the Ah receptor. The use of TEFs and the assumption of additivity have been approved by both the World Health Organization and the U.S. EPA as a default, but interim, approach given the enormity of the task to test for all possible interactions of complex mixtures and in the relative absence of consistent data to the contrary (*94*). Clearly, the TEF values and assumptions regarding additivity need to be updated as more data become available.

Estimates of body burdens in animals and humans assume that the half-life of elimination of dioxins is a first-order process which is independent of the body burden or dose. There is significant evidence that disposition of TCDD is dose dependent (*95–97*). Induction of a binding protein in the liver has been proposed by Andersen et al. (*98*) to explain the dose-dependent disposition of TCDD seen in experimental animals. Similar dose-dependent hepatic sequestration has been proposed in humans (*62*). These data suggest that elimination of these chemicals may not be a first-order process and the use of a single one-component half-life to estimate body burdens may not adequately predict these values.

Two different methods were used to estimate body burdens in experimental animals. One method involved classical pharmacokinetic calculations, and the second method used tissue concentration data presented in the papers. These methods resulted in similar body burden estimates for some cases where the appropriate data were available. For example, in mice receiving 1.5 ng TCDD/kg/day, estimated body burdens using classical pharmacokineti-

calculations were 14 ng TCDD/kg body weight and 23 ng TCDD/kg body weight using TCDD tissue concentrations. Body burden estimates from a tumor promotion study with rats receiving 125 ng TCDD/kg/day produces estimates of 3615 ng TCDD/kg body weight using pharmacokinetic calculations and 2582 ng TCDD/kg body weight using TCDD tissue concentrations. These results suggest that the use of either method to derive body burdens will result in reasonably accurate estimates.

In estimating human body burdens, we assumed that dioxins distribute solely to the lipid portion of the body and that the concentration of dioxins in serum lipid is directly correlated to the concentration of dioxins in total body lipid. Several studies have demonstrated direct correlation between lipid-adjusted serum and adipose tissue concentrations of dioxins from human biopsy samples for the lower chlorinated dibenzo-*p*-dioxins and dibenzofurans (*30–33*). This relationship is not as certain for the higher (six or more chlorine substitutions) chlorinated analogs. Furthermore, in humans exposed to background levels of dioxins, the absolute or lipid-adjusted concentrations of CDDs and CDFs in adipose tissue and liver are not directly related and liver/fat ratios vary between 1.22 and 15.42 depending on the congener and possibly on dose (*99*). The highly chlorinated dibenzo-*p*-dioxins and dibenzofurans are found in greater concentration in the liver compared to the fat (liver/fat ratio 7.4–15.42). In the same samples, TCDD had a liver/fat ratio of approximately 2 (*96*). The human liver appears to accumulate these chemicals in greater proportion than adipose tissue, similar to what has been observed in experimental animals. In experimental animals, liver/fat concentration ratios are not only different for different compounds, but they are dose dependent. As the dose of dioxins are increased, so is the liver/fat ratio (*95–98*).

Using the assumption that dioxins are equally distributed in the body lipid may underestimate the body burden of these chemicals due to chemical and dose-dependent sequestration in the liver. The magnitude of underestimation can be determined if several assumptions are used: that the liver/fat ratio for all dioxins is 15 and that liver is 10% of the body weight and is 10% lipid by weight. A liver/fat ratio of 15, as determined for the hexachlorodibenzofurans in humans, is used as a worst-case scenario for hepatic sequestration. Using these assumptions, the present estimate of dioxin TEQ body burdens in background populations will change from 13 to 21 ng TEQ/kg body weight. Hence, the assumption that dioxins are equally distributed in body lipid may slightly underestimate the body burdens of these chemicals, but the magnitude of error will be less than a factor of two. A better understanding of the pharmacokinetic properties for this class of compounds in humans is clearly indicated.

Chloracne has been described as the hallmark of dioxin toxicity in humans (*17*). Dioxin exposure in several animal species results in a chloracnegenic response and the body burdens which produce this response in animals are similar to the body burdens of dioxins in humans with chloracne. The chloracnegenic response has been thought to be a relatively high-dose phenomenon; however, the variation in human sensitivity to the chloracnegenic effects of TCDD is almost two orders of magnitude. For example, there are individuals who developed chloracne at body burdens approximately three times background (*51*). In contrast, there are subjects with body burdens of 1450 ng TEQ/kg body weight who have not developed chloracne (*51*). These data suggest that humans differ widely in sensitivity to the chloracnegenic actions of dioxins.

There are two points of caution when interpreting the chloracne data. First, human body burdens may not be an accurate measure of chloracnegenic potential if point-of-contact concentrations are important. For example, if dermal exposure results in a localized chloracnegenic response, body burdens estimated from serum or adipose tissue levels may not accurately reflect the concentration of dioxins at the site of effect. Also, the lack of chloracne in highly exposed patients does not necessarily indicate that these individuals are resistant to all the effects of dioxins. In mice, gene products, in addition to the Ah receptor, regulate the chloracnegenic response (*100*). It seems likely that multiple genetic factors may influence the relative susceptibility of individuals in a response-specific fashion.

Human responses to dioxins other than chloracne are not as obvious. In the Yu-Cheng poisoning incident, increased rates of toxic effects such as miscarriages, stillbirths, low birth weight infants, and developmental delays have been observed in offspring of women exposed to high levels of PCDFs and PCBs. However, it has been difficult to determine if the effects are due to the dioxins in the mixture, the nondioxinlike PCBs, or to the combination of these chemicals. Researchers have tried to correlate effects with serum concentrations of either the PCDFs or PCBs (*56*). Birth weights were negatively correlated with PCDF levels in these individuals (*56*). Other effects such as induction of arylhydrocarbon hydroxylase activity, a marker for CYP1A1, were not correlated with either the polychlorinated dibenzofurans or the PCB concentrations, but decreased placental EGF receptor autophosphorylation was correlated with total PCB concentrations (*56*). However, due to the nature of the exposure, patients with high levels of dibenzofurans will likely have high levels of PCBs, making such correlations difficult to interpret. Also, the presence of dioxinlike and non-dioxinlike PCBs adds to the complexity of these correlations.

We compared the body burdens of dioxins in the Yu-Cheng population to body burdens in experimental animals to determine the role of dioxins in the toxic effects seen in these individuals. Women who were pregnant at the time of exposure or became pregnant thereafter had children with lower birth weights compared to unexposed women, and the decrease in size persisted years after birth (*63*). Body burdens in the Yu-Cheng mothers were estimated at 2130 ng TEQ/kg. In experimental animals the body burdens that result in decreased birth weights range from 400 to 2000 ng TCDD/kg, while decreased growth occurs in rats at 1,000 ng TCDD/kg. The similarities between the body burdens in animals and humans suggests that dioxins may play a role in the decreased birth weights.

The behavioral effects of dioxins have not been thoroughly studied in experimental animals. One study reported deficiencies in object learning in rhesus monkeys prenatally exposed to TCDD. Delayed developmental milestones were seen in children born to Yu-Cheng mothers, but the body burdens are approximately 51 times higher in humans than in the monkeys. There is recent evidence that some of the non-dioxinlike PCBs may have neurotoxic actions (*101*). The absence of studies in experimental animals examining the developmental behavioral toxicity of dioxins makes it difficult to assess the role of either the dioxins or the non-dioxinlike PCBs in the developmental effects of the children of the Yu-Cheng patients.

In experimental animals, some biochemical changes produced by dioxins occur at lower body burdens than do the toxic effects (*57–61, 71*). Induction of CYP1A1 and decreased hepatic EGF receptor are two well-characterized biochemical responses to TCDD. Earlier studies comparing the induction of CYP1A1 and decreased EGF receptor in human placenta and rat liver suggested that humans may be more sensitive when compared on a tissue-dose basis (*18*). However, it is possible that the difference in sensitivity is not entirely due to species differences but due to altered tissue sensitivity. For example, induction of CYP1A1 is similar in lung, liver, and skin

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of mice based on administered dose (*102*). In contrast, when the sensitivity of these tissues is compared on a tissue-dose basis, the lung is much more sensitive than the liver or skin (*102*). The present study indicates that humans and rats are equally sensitive to TCDD-induced biochemical changes when compared on a total body burden. Thus, when comparing the relative sensitivity of human or animal tissues to TCDD-induced biochemical changes, it may be more appropriate to compare body burdens than tissue concentrations. In addition, these data provide support for our approach.

TCDD is clearly carcinogenic in experimental animals. All species and both sexes of experimental animals that have been chronically exposed to TCDD exhibit a dose-dependent increased incidence of tumors (*5*). Several recent epidemiological studies have indicated an association between TCDD serum concentrations and increased incidence of tumors (*19–23*). Body burdens in rats and mice with increased tumors are comparable to the body burdens in the human cohorts that have increased incidence of tumors thought to be associated with dioxin exposure. Although these data are not conclusive, they are consistent with the hypothesis that exposure to TCDD was an important factor in the increased incidence of tumors in these cohorts. It is interesting to note that based on body burdens, mice are more sensitive to the carcinogenic effects of TCDD than are rats.

Carcinogenic responses are seen in hamsters, but the carcinogenic doses produce body burdens 46–1,300 times that seen either in humans, rats, or mice. Hamsters are insensitive to the lethal effects of dioxins, and they may also be less sensitive to the carcinogenic response. However, responses such as cancer are dose dependent as well as time dependent. Thus, the apparent differential sensitivity of the hamster may be due to differences in the dose–time regimens used in the hamster compared to the rat and mouse studies. It would be useful to compare these species under similar exposure protocols.

Decreases in serum testosterone have been reported in a National Institute of Occupational Safety and Health (NIOSH) cohort (*41*). There was a decrease in testosterone concentrations in individuals with serum concentrations of TCDD as low as 20 ppt at the time of tissue sampling, which is 3-4 times background TCDD levels and only a 33% increase over total average body burdens. Although the decrease in testosterone concentrations was statistically significant, the decrease was minor, and average levels were still within the normal range. In addition, a clear association between serum TCDD concentrations and effect was not readily apparent in the data (*41*). If differences in exposure patterns in the individuals are taken into account by back-calculating serum TCDD concentrations to the time of exposure, there is a clearer association between serum TCDD concentrations and lower testosterone concentrations. Here the lowest serum TCDD concentration associated with decreased testosterone concentration is 140 ppt (200 ppt TEQ). In experimental animals, high doses of TCDD decrease testosterone concentrations in rats at a body burden of 12,500 ng TCDD/kg body weight (*73*). These data suggest that some humans may be approximately 280 times more sensitive to the testosterone-decreasing effects of dioxins compared to rats. Alternatively, the decreased testosterone levels in the NIOSH cohort could be related to the concomitant exposure to other chemicals involved in the manufacturing process. Future studies examining the sensitivity of other species to the testosterone-decreasing effects of dioxins and epidemiological studies of other populations may provide additional information to adequately assess the association between dinxin exposure and decreased testosterone concentrations in some human populations.

Many of the effects of TCDD have been studied following an acute exposure in experimental animals. In contrast, humans receive low daily doses of these chemicals. One of the assumptions in extrapolating these effects to humans is that the effects are solely related to body burdens. For some of these endpoints, such as decreased testosterone, this assumption has not been adequately tested. Effects such as cancer are clearly related to both dose and time. It is possible that, in addition to dose and body burden, length of exposure may also have a significant effect on toxicity. Analysis of the area under the total body concentration–time curve may be a more appropriate marker for dose, and analysis of these data sets is ongoing.

The clinical significance of some of the endpoints studied is uncertain. Induction of CYP1A1 and CYP1A2 by TCDD are some of the most sensitive markers of dioxin exposure, yet their relevance to toxicity is unclear. Recent studies have suggested an association between PAH exposure and CYP1A1/1A2 induction for lung and colorectal cancer and athelernsclerosis (*103–105*). However, these associations are speculative and not proven. At present, one could conclude that low doses of dioxins produce effects such as enzyme induction in experimental animals and that humans are exposed to levels of dioxins that induce CYP1A1/1A2 in experimental animals, but the relationship between these effects and disease are uncertain.

One of the most sensitive targets for TCDD toxicity in experimental animals is the immune system. Immune alterations, including increased viral sensitivity in mice and altered lymphocyte subsets in marmosets, have been reported at body burdens equivalent to human background exposures. However, the evidence for immunotoxicity of dioxins in humans is inconclusive. There are reports of subtle immune alterations in populations heavily exposed to dioxins. The incidence of intestinal and upper respiratory tract infections correlated with chloracne state and increased with increasing serum TCDD concentrations (*106*). One year after the Yu-Cheng poisoning episode, patients exhibited decreases in percentage of total T-cells, active T-cells, and T-helper cells, which recovered by the 3-year follow up study (*107*). Recent studies of occupationally exposed individuals with slightly elevated body burdens of approximately 72 ng TEQ/kg showed no alterations in lymphocyte subsets (*108*). However, in mice, a dose of TCDD that suppresses the antibody response to sheep red blood cells is not associated with alterations in lymphocyte subsets (*109*). Thus, immune function may be altered without altering lymphocyte subsets. Although some of these data suggest that the human immune system may be sensitive to the effects of dioxins, our present understanding of immunology does not support a conclusion that these alterations are or are not clinically significant.

The present study indicates that *in vitro* similar responses are seen in human and animal tissues after similar dioxin exposure. Human populations exposed to high concentrations of dioxins exhibit symptoms that are similar to the signs of toxicity seen in some experimental animals exposed to dioxins. These effects are seen at equivalent body burdens, strongly indicating that dioxins are responsible for some of these toxic effects in humans. For most of the toxic effects of dioxins, background exposure is well below those associated with overt toxicities. However, the background level used in this evaluation (13 ng TEQ/kg body weight) is an average background. Body burdens of dioxins appear to be log-normally distributed in humans (*110*), thus it would not be unusual to see populations with body burdens three to four standard deviations beyond the mean body burden. Recent studies in the Netherlands indicate that plasma TEQ concentrations in the 95th percentile of the

population are twice that of the mean (*113*), suggesting that at least 5% of the population has two times the mean body burden. In addition, there are subpopulations such as subsistence fishermen who are likely to have much greater body burdens. There are also some toxic effects, such as endometriosis and increased viral sensitivity, which occur in experimental animals at body burdens less than 10 times the average background exposures to humans. Finally, human exposures that result in adverse health effects, such as chloracne, decreased birth weights, developmental delays, and cancer are 3–540 times the present average background exposure to these chemicals. Nevertheless, the available data indicate that high-level human exposure to dioxins produce adverse health effects and that humans are a sensitive species to the toxic effects of dioxins. Whether these low-dose effects are occurring in the general population or the more highly exposed subpopulations remains to be determined.

Appendix. Table Notes

(Some notes appear in more than one table.)

Table 1

a) Apparent equilibrium binding dissociation constants are presented (*42*). Under conditions of infinite dilution, an apparent K_d of 9 pM has been determined for the *Ah*^{b} allele in the C57Bl/6 mice; this value is close to the estimated true K_d (*43*).

b) Splenic lymphocytes from C57Bl/6 mice and peripheral blood lymphocytes were isolated, cultured, and exposed to TCDD. Ethoxyresorufin-O-deethylase (EROD) activity, a marker for CYP1A1, was determined following TCDD exposure (*43*).

c) The authors (*47*) compared the cytotoxic effects of TCDD on organ culture of human, mouse and rat embryonic palatal shelves. Embryonic palates from human, mouse and rat were grown in the same organ culture system and exposed to TCDD. Cytotoxicity was detected using transmission electron microscopy.

d) Thymocytes were isolated from either murine or human sources and cocultured with either murine (*48*) or human (*49*) thymic epithelium culture. The incorporation of tritiated thymidine into DNA was determined in cells treated with TCDD following antigen stimulation.

e) Human tonsilar lymphocytes and murine splenic lymphocytes were used as a source of B-cells. Human and murine B-cells were grown under identical conditions and exposed to TCDD. Proliferation and IgM secretion were determined in response to different concentrations of TCDD ranging from 0.3 to 30 nM (*50*).

Table 2

f) The lower value, 96 ng TEQ/kg body weight, is the body burden estimate of a patient with the lowest reported adipose dioxin concentration for any patient with chloracne (*51*). This individual was exposed to a mixture of CDDs and CDFs in 1969 and developed chloracne. At the time of exposure this individual had adipose tissue CDD/CDF concentrations of 419 ng TEQ/kg adipose tissue (*51*). An additional 17 ng TEQ was added to this value to include the PCBs. The values of dioxins at the time of exposure were estimated by the authors (*51*). The higher of the two values represents the average body burden of dioxins (TEQs) in individuals from Yusho with chloracne (*52*). Estimates of body burdens from these individuals were determined by Ryan et al. (*52*).

g) Rhesus monkeys were administered 1 µg/kg TCDD, and it is assumed that essentially no TCDD was eliminated when the animal developed a chloracnegenic response. This is a LOEL dose; no lower doses were tested (*53*).

h) Assumes the rabbit and the rat have the same rate of elimination, a half-life of 23.7 days (*88*) and that the rabbits weighed 2.5 kg throughout the experiment. This is a LOEL dose; no lower doses were tested (*52*).

i) Assumes the half-life of TCDD in mice is 11 days and that the mice weigh 25 g. This is a LOEL dose; no lower doses were administered (*5*).

j) In highly exposed patients from the Yu-Cheng incident, there is a decrease in birth weights of children born from these patients compared to unexposed control populations (*18,56*). In addition, the Yu-Cheng mothers have altered levels of placental epidermal growth factor receptor (EGFR) and CYP1A1. The data indicate that the changes in placental EGFR and CYP1A1 in these patients were maximal. Body burdens determined based on levels of 2,3,4,7,8-pentachloro-dibenzofuran (TEF = 0.5) and 1,2,3,4,7,8-hexachlorodibenzofuran (TEF = 0.1) in placenta tissue. Lipid content of the placenta is estimated at 1% (*112*) and the average percent body fat of a women is assumed to be 22%. These body burden estimates were also used as body burdens of Yu-Cheng mothers whose children demonstrate decreased growth (*63*) and delayed developmental milestones (*64,65*).

k) in a rat liver tumor promotion study, rats initiated with diethylnitrosamine were exposed to doses of TCDD from 3.5 to 125 ng/kg/day. Statistically significant increases in numbers of altered hepatic foci were observed in rats treated with 125 ng TCDD/kg/day (*67*). At the end of the study, liver concentrations of TCDD were approximately 20 ppb (*60*); assumes 20% body weight is adipose tissue and that at this dose, the liver has three times the concentration of TCDD than adipose tissue. Body and liver weights were reported (*67*) for these animals. The body burden calculation assumes that liver and fat account for 85% of the body burden in these animals. For tumor promotion, 125 ng TCDD/kg/day is the LOEL and 35 ng TCDD/kg/day is the NOEL for tumor promotion (*67*). For induction of CYP1A1 (*60*) and downregulation of EGFR (*59*), 125 ng TCDD/kg/day was assumed to produce a maximal response.

l) Mice were administered 10 µg TCDD/kg and sacrificed 7 days after treatment. EGFR binding was determined in hepatic plasma membrane (*58*).

m) Animals received a single dose and were sacrificed 24 hr later. Assumes no TCDD eliminated at this time CYP1A1 induction determined by RT-polymerase chain reaction (*60*). The LOEL for CYP1A1 induction was 1 ng/kg, a no observed effect level from this study is 0.1 ng/kg.

n) Animals received 1.5 ng/kg/day 5 day/week for 13 weeks (*61*). Mice were sacrificed 3 days after last dose. Hepatic, dermal, and pulmonary EROD activity were significantly induced at this dose. Tissue concentrations of TCDD were measured in liver, skin, and fat. Body burden estimates assumes 95% of the body burden is in liver, skin, and fat. This is the LOEL from this study; no lower doses were tested.

o) Body burdens are estimated by authors (*62*) for the increased accumulation of PCDD/PCDF in liver compared to adipose tissue using a pharmacokinetic model.

p) Assumes average level of dioxins and dibenzofurans in human serum ranges from 28 to 41 TEQ ppt and from 8 to 17 TEQ ppt for the PCBs. Thus, the average TEQ ranges from 36 to 58 TEQ ppt. Using 58 ppt as the average concentration of PCDDs, PCDFs, and PCBs in serum, a body burden of 12.76 ng TEQ/kg body weight was calculated

For PCDD and PCDF concentratinns, a body burden of 9 ng TEQ was determined. Average concentrations of TCDD in adipose tissue are 5 ppt (lipid adjusted) (*27*), resulting in a body burden of 1.1 ng TCDD/kg.

q) In control rats, PCDDs and PCDFs were determined at different ages; 200-day-old rats had approximately 78 ppt TEQs in liver (*67*). This is an equivalent liver concentration in 60-day-old rats 24 hr after administration of 1 ng TCDD/kg.

r) Liver, fat, blood, and skin concentrations of TCDD, 1,2,3,7,8-PCDD, 2,3,7,8-TCDF, 1,2,3,7,8-PCDF, 2,3,4,7,8-PCDF, and OCDF were determined in 150-day-old female B6C3F_1 mice. The TEF methodology was used to estimate TEQ levels in these animals; assumes that 95% of the body burden is in liver, fat, and skin.

Table 3

s) Estimated highest body burden at time of last exposure. Calculations based on measured TCDD levels in serum (lipid adjusted) and assuming a first-order elimination kinetics and a half-life for elimination of 7.1 years. Also assumes a body weight of 70 kg and 22% body fat. Calculations for estimated serum concentrations at last time of exposure performed by authors (*18,23*).

t) Animals administered 100 pg TCDD/kg 6 times every 4 weeks over a 24-week period; assumes a half-life of 14.9 days (*111*). Body burdens are estimated immediately after the last treatment with TCDD. The administration of 50 µg TCDD/kg 6 times every 4 weeks over a 24-week period did not increase the incidence of any types of tumors in 10 hamsters (*68*).

u) Assumes a single first-order elimination rate constant and a half-life for the whole body elimination of 23.7 days (*85*) and a gastrointestinal tract absorption of 86% (*85*). Increased incidence of hepatocellular carcinomas were observed at 100 ng/kg/day and 10 ng/kg/day is the NOEL (*69*). Decreased testis weight and testosterone concentrations were observed after 12.5 ng TCDD/kg 7 days later (*76*). Decreased serum glucose levels were observed in rats treated with 100 ng/kg/day for 30 days (*79*).

v) Assumes an apparent half-life of 11 days and a body weight of 20 g. Mice receiving 71.4 ng/kg/day for 2 years had a statistically significant increase in hepatocellular carcinomas (*70*).

w) Assumes neonatal rats and hamsters are exposed to an equal dose of TCDD as are the dams on a weight basis and assumes all alterations are due to the neonatal exposure. For decreased body weight in pups 400 ng/kg is the LOEL; a dose of 64 ng/kg to the dam was the NOEL for this response (*73*). For decreased sperm count the LOEL is 64 ng/kg and no lower doses were tested (*86*). In hamsters only one dose was tested (2000 ng/kg) for decreased sperm counts (*74*). Decreased growth in rats is indicated by decreased body weights up to postnatal day 63 (*75*). The incidence of fetal mortality was increased in hamsters at a dose of 18 µg/kg but not at a dose of 6 µg/kg (*81*).

x) Assumes a single first-order elimination rate constant and a half-life for the whole-body elimination of 400 days (*81*) and a gastrointestinal absorption of 86% (*88*). This is the LOEL from this study; no lower doses tested. Monkeys exposed to a diet of approximately 5 ppt had a daily intake of 0.151 ng/kg/day. Monkeys exposed to approximately 25 ppt in the diet had a daily intake of approximately 0.76 ng/kg/day. For animals with decreased object learning, the TCDD-exposed offspring were born after 16.2 months of maternal TCDD exposure of a diet of 0.151 ng TCDD/kg/day. Animals with increased incidence and severity of endometriosis had a daily intake of 0.151 ng/kg/day for 4 years, and body burdens were determined at the end of the exposure period. Monkeys exposed to 0.76 ng TCDD/kg/day for 16.2 months had significant decreases in offspring viability.

y) The authors extrapolated serum concentrations of TCDD at the time of sampling to initial exposures (*41*). Workers with serum TCDD concentrations of 140–496 ng/kg (lipid adjusted) have a greater incidence of low testosterone concentrations (*41*). Extrapolation assumed a half-life for TCDD of 7.1 years. To estimate body burdens in these workers, it was assumed that the background TEQ was 60 ng/kg, thus the total serum TEQ was 140 ng TCDD/kg + 60 ng TEQ/kg = 200 ng TEQ/kg (lipid adjusted).

z) Assumes that high-exposed group (>33 ng/kg) had a background of 60 TEQ ng/kg. This group had at least 93 TEQ ng/kg. Assumes average subject was male, weighing 70 kg with 22% body fat.

aa) Workers with increased glucose tolerance and diabetes have serum levels of 640 ppt TEQ (*24*).

bb) Guinea pigs received 30 ng TCDD/kg intraperitoneally and sacrificed 24 hr after dose. Assumes that no TCDD was eliminated at this time. This is a LOEL, no other doses tested (*78*).

Table 4

cc) Assuming a single first-order elimination rate constant and a half-life of 6–8 weeks. Body burdens calculated by authors (*82*). Animals treated with a single dose of TCDD were tested 2 weeks after treatment (*83*).

dd) Mice were treated with TCDD and challenged with influenza virus 7 days later (*84*).

ee) Mice were administered 100 pg/kg and examined 30 days after receiving the treatment (*77*).

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Exposure to Polychlorinated Dioxins and Furans (PCDD/F) and Mortality in a Cohort of Workers from a Herbicide-producing Plant in Hamburg, Federal Republic of Germany

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The relation between mortality (all cause; cancer; cardiovascular diseases (*International Classification of Diseases*, Ninth Revision (ICD-9), codes 390–459); ischemic heart diseases (ICD-9 codes 410–414)) and exposure to polychlorinated dibenzo-*p*-dioxins and -furans (PCDD/F) was investigated in a retrospective cohort study. The cohort consisted of 1,189 male workers in a chemical plant in Hamburg, Federal Republic of Germany, who had produced phenoxy herbicides, chlorophenols, and other herbicides and insecticides known to be contaminated with 2,3,7,8-tetrachlorodibenzo-*p*-dioxin and other, higher chlorinated dioxins and furans. The authors reported previously on cancer mortality in this cohort for the follow-up period 1952–1989. The current study covers the years 1952–1992 and investigates the relation of PCDD/F exposure to mortality using a quantitative estimate of PCDD/F exposure for the whole cohort derived from blood and adipose tissue levels measured in a subgroup (n = 190). Quintiles and deciles of these estimates served as dose parameters in the estimation of relative risks (RRs), using year-of-birth stratified Cox regression. An unexposed cohort of gas workers served as an external reference group. The total mortality was elevated in all dose groups. The highest relative risk was observed for the highest 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) decile (RR = 2.43, 95% confidence interval (CI) 1.80 to 3.29). Cancer mortality and mortality due to ischemic heart diseases showed a dose-dependent relation with TCDD and all PCDD/F combined. The highest relative risks for cancer (RR = 3.30, 95% CI 2.05 to 5.31) and ischemic heart diseases (RR = 2.48, 95% CI 1.32 to 4.66) were observed in the highest PCDD/F exposure group. The pattern of effects and tests for trend were similar when the lowest exposure group within the chemical worker cohort served as the reference, but the relative risks were smaller and the confidence intervals were larger. Potential confounding exposures complicate the interpretation of the internal comparison. These findings indicate a strong dose-dependent relation between mortality due to cancer or ischemic heart diseases and exposure to polychlorinated dioxins and furans. *Am J Epidemiol* 1995; 142:1165–75.

dioxins; mortality; myocardial ischemia; neoplasms; occupational exposure

2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD) is a widespread environmental contaminant in food, soil, and water. It produces a variety of toxic effects in experimental animals at very low doses, including carcinogenicity, immunotoxicity, teratogenicity, disturbances of lipid metabolism, and biochemical effects involving drug-metabolizing enzymes (1).

However, there is an ongoing debate concerning the susceptibility of humans to toxic effects of this substance. It is widely agreed that TCDD causes chloracne in dose ranges comparable to those observed in experimental animals. The first reports on this issue were published in 1957 (2) and 1964 (3). With respect to carcinogenicity in humans, three epidemiologic studies with an exposure assessment partly based on dioxin levels in blood (from a subgroup) have found similar associations. A large US study (4) and a smaller German study (5) reported elevated risks of total cancer mortality in groups of workers with substantial exposure to TCDD (verified by measurements of blood concentrations) and a latency time of about 20 years. Our group reported an elevation of total cancer mortality for a cohort of workers [illegible]

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Abbreviations: CI, confidence interval; ICD-9, *International Classification of Diseases*, Ninth Revision; PCDD/F, polychlorinated dibenzo-*p*-dioxins and -furans; RR, relative risk; TCDD, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin.

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ical plant in Hamburg (n = 1,184 men) that produced herbicides contaminated with TCDD and other polychlorinated dioxins and furans (6). The follow-up period was 1952–1989. The relative risks varied with the polychlorinated dibenzo-*p*-dioxin and -furan (PCDD/F) exposure surrogate (duration of employment, time of entry into the plant, qualitative exposure groups). In a subsequent analysis (7), it was shown that the duration of employment in different production departments with different levels of exposure was quantitatively related to cancer mortality. Significantly elevated relative risks for cancer mortality were observed for the departments with the highest TCDD exposure. However, no dose-response relations in terms of quantitative PCDD/F exposure levels could be estimated.

The experimental and epidemiologic evidence for a potential relation of cardiovascular diseases, especially ischemic heart diseases, to PCDD/F exposure is less compelling than that for cancer. There are, however, a number of reports suggesting that TCDD may influence a number of risk factors for ischemic heart diseases. This possible link was addressed in several epidemiologic studies investigating outcomes related to ischemic heart diseases: prevalence of ischemic heart diseases (8–11), hypertension (9, 10, 12), blood lipid disturbances (9, 10, 12–16), and diabetes (17, 18). However, no definite conclusion can be drawn from these studies because of inconsistencies in findings, uncertainties about exposure, and possible selection bias. Several animal studies also investigated the effects of TCDD exposure on cardiovascular outcomes. The reported effects include morphological changes in peripheral vessels (19, 20), functional disturbances (21–23), and disturbances in lipometabolism (24–27).

Since our first report on the cohort of chemical workers from Hamburg, new data have been collected. These new data include an increase in the number of cohort members with determinations of PCDD/F in the blood, data on the elimination velocity of PCDD/F, and extension of mortality follow-up from 1989 to 1992. These new data allow the construction of quantitative PCDD/F exposure indicators. This paper reports the findings on the quantitative relations between total mortality and mortality due to cancer, ischemic heart diseases, cardiovascular diseases, and all other causes and these new PCDD/F exposure indicators.

MATERIALS AND METHODS

The cohort consisted of all regular employees of a chemical plant in Hamburg, Germany, employed for at least 3 months between 1952 and 1984 when the plant was closed. Workers were identified by company personnel and union election records and by information obtained from employees. The mortality follow-up reported here covered the years 1952–1992.

Exposure assessment

Exposure to PCDD/F in the plant had occurred in the production of different herbicides and insecticide (2,4,5-trichlorophenoxyacetic acid, trichlorophenol, Bromophos, lindane; for details see reference 6).

For the analysis of the relation between PCDD/F exposure and different mortality outcomes, a quantitative exposure variable, describing the chronic occupational exposure to PCDD/F in terms of the estimated PCDD/F blood levels at the end of exposure above German background levels, was constructed as follows. First, definitions of 14 production departments of the plant were developed from an analysis of the production processes by an industrial hygienist. These definitions included measurements of PCDD/F levels in the various products of the plant, in waste products and in different buildings within the plant. Second, each worker was assigned the time (in years) he had worked in each of the 14 production departments or areas (e.g., trichlorophenoxyacetic acid production). These duration estimates were derived from personnel records supplied by the company and additional information elicited from workers in personal interviews (for details see reference 28). Third, concentrations of PCDD/F in adipose tissue (n = 48 (29)) or whole blood (n = 142) were determined for 190 male workers. Some of these data (n = 121) have been described previously (30). Fourth, adopting the standard assumptions of a one-compartment first-order kinetic model, we estimated PCDD/F levels at the end of exposure ($PCDD/F^{endex}$) for the 190 workers with available determinations of PCDD/F at various time points. This estimation used the half-lives calculated from an elimination study in 48 workers from this cohort (31) and background levels for the German population (32). The contribution of the working time in each production department on $PCDD/F^{endex}$ was then estimated using ordinary least-squares regression through the origin according to the equation

$$PCDD/F_i^{endex} = \sum_{j=1}^{k} \beta_j \times x_{ij} + \epsilon_i \qquad (1)$$

where x_{ij} denotes the working time (in years) for the ith worker in the jth production department. Finally, using the values of x_{ij} available for all workers in the cohort and the values of β_j obtained from the subgroup with blood/tissue PCDD/F levels, we calculated the estimated PCDD/F levels for all members of the cohort for each congener. A total toxic equivalence was

able was also computed for all dioxins and furans combined. This variable was calculated as the weighted sum of all congeners, where the weights were toxic equivalency factors expressing the toxicity of each congener relative to that of TCDD (33).

Exposure to other carcinogens or suspected carcinogens had occurred in some production departments of the plant. Of special importance was exposure to the known carcinogen dimethyl sulfate in the opiate department where morphines had been produced. Additionally, exposure to different isomers of hexachlorocyclohexane, some suspected to be carcinogenic, had occurred in the departments involved in the production and formulation of lindane. Finally, there had been exposure to benzene, especially in the synthesis of hexachlorocyclohexane. However, all these exposures occurred in production departments with low- to mid-range exposure to TCDD and other PCDD/F.

Reference group

An external control cohort served as an unexposed reference group. The importance of including a comparison group stems from several considerations. First, while chemical workers with lengthy work durations in heavily contaminated production departments are probably classified correctly with respect to PCDD/F exposure, workers with shorter durations of work in "low exposure" departments could be subject to a higher probability of misclassification. Second, there is a potential for negative confounding within the cohort. This is especially problematic with respect to cancer mortality, since exposure to other carcinogens had occurred in the low PCDD/F exposure groups. Finally, the inclusion of unexposed controls increases the power of the study.

The reference group consisted of a cohort of workers from a gas supply company from the same region of Germany as the chemical worker cohort. The control cohort was formerly investigated by some of us following the same methods in assessing vital status and causes of death. This group had served as an internal reference group of "blue-collar workers" in a cancer mortality study of coke oven workers (34). The socioeconomic status of the gas worker and chemical worker cohorts is comparable. The follow-up period for the reference group was set from 1952 to 1989. A detailed description of this referent cohort was reported elsewhere (34). No special exposure to PCDD/F is known to have occurred, so each worker of the referent cohort was assigned a PCDD/F level of zero above German background levels.

Assessment of causes of death

Vital status was assessed by direct contact or through community registries. Causes of death were derived from records obtained from a hospital or family doctor by a pathologist. Causes of death were coded according to the *International Classification of Diseases*, Ninth Revision (ICD-9), by an experienced nosologist. If no records were available, death certificates or other information (life insurance records, next of kin) was used. The quality of the determinations of underlying cause of death was assessed for ICD-9 codes 390–579. Available medical records or death certificates were reviewed for 138 of 162 members of the chemical worker cohort and a random sample ($n = 32$) of the control cohort. The review was conducted by an independent pathologist who was blinded to cohort membership. The validity of cancer death determinations was reported earlier (6).

Risk estimation

Relative risks were estimated with year-of-birth stratified (5-year intervals) Cox regression, using seven exposure levels (the referent cohort, the first four quintiles, and the ninth and 10th deciles of the estimated TCDD levels and total toxic equivalencies for the chemical worker cohort. Persons with unknown vital status were excluded from the analyses. Tests for trend were performed as suggested by Rothman (35). The calculations were performed with the Statistical Analysis System (SAS) procedure PHREG (36). Because of differences between the cohorts in the distribution of total duration of employment, age, and year at which employment began, the relative risks were adjusted for these covariates. In addition, an internal comparison within the chemical worker cohort was performed using the two lowest quintiles with respect to TCDD and total toxic equivalencies as reference category. To assess the potentially confounding effect of exposure to other carcinogens, a subanalysis with regard to cancer mortality was conducted by excluding workers potentially exposed to dimethyl sulfate.

RESULTS

Exposure

Results of regressions of PCDD/F levels on duration of work in each production department are given in table 1 for 190 chemical workers with blood/tissue determinations. The Pearson correlation coefficient between model-predicted and measured TCDD levels was $r = 0.46$ ($p < 0.01$). The duration of employment in the trichlorophenoxyacetic acid and the 2,4,5-trichlorophenol (before 1957) departments showed the

TABLE 1. Estimated yearly increase (ng/kg of blood fat) in TCDD* and TEQ* (without TCDD) levels due to working times in different production departments: Hamburg, Germany, 1952–1992

Production department	TCDD	TEQ
2,4,5-Trichlorophenoxyacetic acid	75.6 (56.0 to 95.2)†	8.5 (−1.9 to 18.9)
Trichlorophenol after or during 1957	39.1 (14.9 to 63.3)	14.5 (1.4 to 27.5)
Trichlorophenol before 1957	292.1 (139.3 to 444.9)	34.0 (−48.8 to 116.8)
Alpha decomposition	0.3 (−29.7 to 30.4)	57.4 (41.7 to 73.2)
Trichlorobenzene	37.7 (−67.4 to 142.8)	39.4 (−16.9 to 95.7)
Bromophos	9.9 (−19.0 to 38.8)	8.1 (−7.4 to 23.6)
Hexachlorocyclohexane synthesis	16.3 (−13.4 to 46.1)	3.2 (−12.3 to 18.7)
Lindane	3.8 (−19.6 to 27.2)	7.2 (−5.3 to 19.7)
Formulation	13.8 (−25.1 to 52.7)	10.4 (−12.5 to 33.3)
Manual workers	12.3 (−2.9 to 27.4)	12.4 (4.4 to 20.4)
Unskilled workers	14.8 (−61.7 to 91.2)	18.8 (−21.2 to 58.8)
Store and transport	−4.2 (−30.8 to 22.3)	5.7 (−8.4 to 19.8)
Administration and others	2.7 (−16.2 to 21.7)	1.3 (−9.8 to 12.4)
Opiate (morphine production)	−0.1 (−57.0 to 56.8)	5.4 (−28.6 to 37.5)

* TCDD, tetrachlorodibenzo-*p*-dioxin; TEQ, toxic equivalencies of polychlorinated dibenzo-*p*-dioxins and furans.

† Numbers in parentheses, 95% confidence interval.

strongest associations with TCDD levels (75.6 and 292.1 ng/kg/year, respectively). Work durations in the 2,4,5-trichlorophenol department in 1957 (when the production procedure was modified to reduce TCDD contamination) or later had a smaller effect (39.1 ng/kg/year). The relation for manual work (12.3 ng/kg/year) was of borderline significance. The estimates for other departments ranged up to 37.7 ng/kg/year (trichlorobenzene), but the standard errors were large. This suggests that an intake of TCDD had occurred in the course of work in these departments, too, but the working times alone provide only imprecise estimates. The negative coefficients for the store and transport department and opiate department cannot be interpreted as the absence of exposure.

For the higher chlorinated dioxins, a significant model fit was obtained with the exception of the hepta congener. The significant correlations between the actual and the estimated PCDD/F levels ranged between $r = 0.17$ for 1,2,3,7,8,9-hexadioxin and $r = 0.79$ for 1,2,3,4,7,8-hexadioxin. A significant model fit for the furans was obtained for 2,3,4,7,8-pentafuran and all hexa congeners except 2,3,4,6,7,8-hexafuran. The correlation coefficients were in the same range as for the dioxins. Expressed as toxic equivalencies, the highest estimated yearly increase in toxic equivalencies (without TCDD) was observed in the thermic decomposition department (57.4 ng/kg/year of toxic equivalencies) and the trichlorobenzene department (39.9 ng/kg/year). A yearly increase of 12.4 ng/kg/year of toxic equivalencies for manual workers was observed. For the trichlorophenol department, since 1957 the estimate was 14.5 ng/kg/year. The confidence intervals for the other departments included zero.

These estimates were then applied to calculate the expected PCDD/F levels for each cohort member at the end of employment in the plant. The duration of employment in each department was multiplied by the effect estimates for the respective departments. This yielded a mean estimated TCDD level of 141.4 ng/kg (median, 38.2 ng/kg) for the cohort. The mean of toxic equivalencies (without TCDD) was 155 ng/kg (median, 69.2 ng/kg), and the mean of toxic equivalencies including TCDD (total toxic equivalencies) was 296.5 ng/kg (median, 118.3 ng/kg).

Mortality

Table 2 summarizes the mortality of the cohorts. Vital status was ascertained for 1,177 of 1,189 (99.0 percent) male chemical workers and for 2,518 of 2,528 (99.6 percent) gas workers. A total of 414 deaths were observed among the chemical workers. No information on the causes of death was available for five deceased workers. Thirty percent of the deaths were attributed to cancer, and 18.4 percent were attributed to ischemic heart diseases. Corresponding percentages in the reference group were 30 percent and 21.7 percent. The sources for diagnoses in the chemical worker cohort were as follows: 34.7 percent from autopsy, 33.7 percent from hospital reports, 25 percent from other medical sources including death certificates, and 6.7 percent from other nonmedical sources, including insurance records and information from family members. The corresponding percentages for the referent group were 29.6 percent from autopsy, 37.0 percent from hospital records, 26.3 percent from other medical sources, and 13.1 percent from other nonmedical sources.

TABLE 2. Number of workers, vital status, and causes of death: Hamburg, Germany, 1952–1992

	Chemical workers		Gas workers	
	No.	%	No.	%
Cohort size	1,189		2,528	
Vital status				
Known	1,177	99.0	2,518	99.6
Unknown	12	1.0	10	0.4
Vital status				
Known	1,177	100	2,518	100
Alive	763	64.8	1,575	62.5
Deceased	414	35.2	943	37.5
Cancer (ICD-9* codes 140–208)	124	30.0	283	30.0
All CVD* (ICD-9 codes 390–459)	157	38.0	459	48.6
IHD* (ICD-9 codes 410–414)	76	18.4	205	21.7
Other CVD	81	19.6	254	26.9
Other causes	133	32.1	201	21.3

* ICD-9, *International Classification of Diseases*, Ninth Revision; CVD, cardiovascular disease; IHD, ischemic heart disease.

The reliability of the study determinations of the cause of death was assessed by a second pathologist. The confirmation rate for cancer deaths among chemical workers was 96.5 percent as reported earlier (6), comparable to that for the referent group (99 percent). The ischemic heart diseases and cardiovascular diseases diagnoses among the chemical workers were confirmed in 77.8 percent and 85.1 percent of the cases, respectively. In the referent group of gas workers, the corresponding confirmation rates were 92.9 percent and 94.1 percent.

Tables 3 and 4, as well as figure 1, summarize the estimated relative risks for the mortality outcomes under consideration. These Cox regression estimates used data from both the chemical worker and control cohorts. The total mortality was elevated in all TCDD and total toxic equivalencies categories, reaching a relative risk (RR) of 2.43 (95 percent confidence interval (CI) 1.80 to 3.29) in the highest TCDD exposure group.

In the case of cancer mortality, the monotonic increase in relation to TCDD is disrupted in the first quintile. While for the lowest TCDD category a relative risk of 1.59 (95 percent CI 1.01 to 2.51) was observed, the estimate for the second quintile was 1.29 (95 percent CI 0.75 to 2.22), increasing to 1.70 (95 percent CI 0.99 to 2.93) in the ninth decile and 3.30 (95 percent CI 2.05 to 5.31) in the tenth decile. The test for trend is highly significant. For total toxic equivalencies, the deviation from a monotonic trend was observed in the second category, but the pattern and the magnitude of estimates are similar to those for TCDD.

While the association is not as strong as that seen with cancer mortality, a clear pattern of increasing risk of cardiovascular diseases and ischemic heart diseases mortality across exposure categories emerges. There is no evidence of increased risk in the two lowest TCDD quintiles. The test for trend is significant for both mortality outcomes. The relative risk of ischemic heart diseases mortality increases from the ninth decile (RR = 1.61, 95 percent CI 0.85 to 3.04) to the 10th decile (RR = 2.48, 95 percent CI 1.32 to 4.66). For total toxic equivalencies, the dose-response pattern with regard to cardiovascular diseases and ischemic heart diseases mortality is more pronounced than that observed for TCDD alone.

Other cardiovascular diseases mortality (nonischemic heart diseases) showed an increase in risk with TCDD up to the fourth quintile, but the risk decreases in the ninth and 10th deciles. The same holds for total toxic equivalencies. The risk of death from causes other than cancer and cardiovascular diseases showed no dose-related trend.

TABLE 3. Relative risk of total, cancer, CVD,* IHD,* other CVD, and other-cause mortality in relation to quintiles (upper quintile divided into deciles) of estimated TCDD* levels (ng/kg of blood fat) at the end of exposure above German median background levels using the cohort of gas workers as reference: Hamburg, Germany, 1952–1992

TCDD	Total mortality	Cancer	CVD	IHD	Other CVD	Other causes
0–2.8	1.0	1.0	1.0	1.0	1.0	1.0
2.81–14.4	1.55 (1.21 to 1.98)†	1.59 (1.01 to 2.51)	1.32 (0.81 to 1.83)	1.43 (0.83 to 2.44)	1.02 (0.54 to 1.92)	1.79 (1.16 to 2.77)
14.5–49.2	1.30 (0.98 to 1.71)	1.29 (0.75 to 2.22)	0.88 (0.54 to 1.44)	0.91 (0.41 to 1.61)	0.98 (0.49 to 1.97)	1.70 (1.07 to 2.70)
49.3–156.7	1.47 (1.14 to 1.90)	1.66 (1.03 to 2.66)	1.35 (0.91 to 2.01)	1.18 (0.65 to 2.16)	1.54 (0.90 to 2.64)	1.38 (0.86 to 2.23)
156.8–344.6	1.48 (1.15 to 1.91)	1.60 (1.02 to 2.52)	1.64 (1.12 to 2.39)	0.98 (0.47 to 1.75)	2.52 (1.57 to 4.04)	1.06 (0.62 to 1.83)
344.7–3,850.2	1.37 (0.99 to 1.90)	1.70 (0.99 to 2.93)	1.53 (0.95 to 2.44)	1.61 (0.85 to 3.04)	1.46 (0.72 to 2.94)	0.71 (0.31 to 1.63)
344.7–1,850.2	2.43 (1.80 to 3.29)	3.30 (2.05 to 5.31)	1.96 (1.15 to 3.34)	2.48 (1.32 to 4.66)	1.34 (0.45 to 1.40)	2.58 (1.15 to 5.81)
p for trend	0.01	0.01*	0.04	0.01	0.72	0.29

* CVD, cardiovascular disease; IHD, ischemic heart disease; TCDD, tetrachlorodibenzo-*p*-dioxin.
† Numbers in parentheses, 95% confidence intervals.

TABLE 4. Relative risk of total, cancer, CVD,* IHD,* other CVD, and other-cause mortality in relation to quintiles (upper quintile divided into deciles) of estimated TOTTEQ* levels (ng/kg of blood fat) at the end of exposure above German median background levels using the cohort of gas workers as reference: Hamburg, Germany, 1952–1992

TOTTEQ concentration	Total mortality	Cancer	CVD	IHD	Other CVD	Other causes
	1.0	1.0	1.0	1.0	1.0	1.0
1.0–12.2	1.45 (1.11 to 1.93)†	1.38 (0.93 to 2.40)	0.73 (0.57 to 1.50)	1.02 (0.54 to 1.95)	0.84 (0.40 to 1.74)	2.04 (1.28 to 3.1
12.3–39.5	1.39 (1.07 to 1.81)	1.71 (1.07 to 2.74)	0.92 (0.59 to 1.46)	0.96 (0.51 to 1.82)	0.91 (0.48 to 1.75)	1.70 (1.06 to 2.7
39.6–66.9	1.54 (1.20 to 1.97)	1.50 (0.93 to 2.42)	1.48 (1.01 to 2.17)	0.97 (0.52 to 1.81)	2.05 (1.26 to 3.36)	1.57 (0.99 to 2.4
69.0–278.5	1.34 (1.04 to 1.74)	1.56 (1.00 to 2.43)	1.55 (1.07 to 2.24)	1.13 (0.64 to 2.00)	2.07 (1.27 to 3.39)	0.72 (0.39 to 1.3
278.6–545.0	1.65 (1.20 to 2.25)	1.71 (0.98 to 2.98)	1.63 (1.01 to 2.64)	1.73 (0.92 to 3.27)	1.53 (0.73 to 3.20)	1.52 (0.81 to 2.8
545.1–4,961.9	2.28 (1.67 to 3.12)	3.27 (2.04 to 5.26)	2.06 (1.23 to 3.45)	2.72 (1.49 to 4.98)	1.19 (0.44 to 3.26)	1.48 (0.72 to 3.0
p for trend	0.01	<0.01	<0.01	<0.01	0.55	0.29

* CVD, cardiovascular disease; IHD, ischemic heart disease; TOTTEQ, toxic equivalencies of polychlorinated dibenzo-*p*-dioxins and furans.

† Numbers in parentheses, 95% confidence interval.

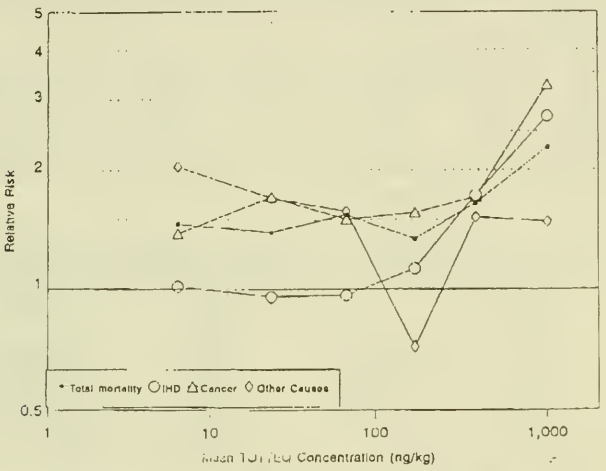

FIGURE 1. Total, cancer, ischemic heart disease (IHD), and other cause mortality in relation to quintiles (upper quintile divided into dec of estimated total toxic equivalence (TOTTEQ) levels above median German background levels using the cohort of gas workers as referer Hamburg, Germany, 1952–1992.

Tables 5 and 6 show the relative risks from calculations using only the data from the PCDD/F-exposed cohort alone. In general, the estimates were lower compared with the analysis including the referent cohort, and the confidence intervals were larger. Total mortality and cancer mortality are elevated in the highest TCDD category. For ischemic heart diseases mortality, the highest risk was also observed in the highest TCDD and total toxic equivalencies exposure groups. The test of trend is significant for ischemic heart diseases and total toxic equivalencies, indicating a dose-dependent relation. Other cardiovascular d eases and other causes showed no dose-related patt in this analysis.

The results of a secondary analysis of cancer mo tality addressing the question of potential confoundi by exposure to dimethyl sulfate in the opiate depa ment are presented in table 7. The 149 workers w nonzero employment durations in this departme were excluded from the analysis. Note that a mo pronounced dose-response pattern for TCDD and to toxic equivalencies is obtained. The effect on canc

TABLE 5. Relative risk of total, cancer, CVD,* IHD,* other CVD, and other-cause mortality in relation to quintiles (upper quintile divided into deciles) of estimated TCDD* levels (ng/kg of blood fat) at the end of exposure above German median background levels (chemical workers only, two lowest categories combined as reference): Hamburg, Germany, 1952–1992

TCDD	Total mortality	Cancer	CVD	IHD	Other CVD	Other causes
0–14.4	1.0	1.0	1.0	1.0	1.0	1.0
14.5–49.2	1.05 (0.80 to 1.38)†	1.24 (0.73 to 2.08)	1.34 (0.85 to 2.10)	1.12 (0.58 to 2.16)	1.59 (0.85 to 2.99)	0.78 (0.49 to 1.24)
49.3–156.7	0.94 (0.69 to 1.26)	1.02 (0.59 to 1.77)	1.25 (0.78 to 1.99)	0.56 (0.31 to 1.41)	2.01 (1.07 to 3.77)	0.65 (0.36 to 1.15)
156.8–344.6	0.83 (0.57 to 1.19)	0.95 (0.50 to 1.81)	1.10 (0.63 to 1.92)	1.18 (0.50 to 2.49)	1.02 (0.45 to 2.31)	0.47 (0.20 to 1.11)
344.7–3,890.2	1.41 (0.97 to 2.05)	2.03 (1.10 to 3.75)	1.28 (0.87 to 2.46)	1.59 (0.71 to 3.56)	0.78 (0.24 to 2.49)	1.31 (0.64 to 2.67)
p for trend	0.20	0.04	0.14	0.18	0.50	0.88

* CVD, cardiovascular disease; IHD, ischemic heart disease; TCDD, tetrachlorodibenzo-*p*-dioxin.
† Numbers in parentheses, 95% confidence interval.

TABLE 6. Relative risk of total, cancer, CVD,* IHD,* other CVD, and other-cause mortality in relation to quintiles (upper quintile divided into deciles) of estimated TOTTEQ* levels (ng/kg of blood fat) at the end of exposure above German median background levels (chemical workers only, two lowest categories combined as reference): Hamburg, Germany, 1952–1992

TOTTEQ concentration	Total mortality	Cancer	CVD	IHD	Other CVD	Other causes
1.19–39.5	1.0	1.0	1.0	1.0	1.0	1.0
39.6–98.9	0.97 (0.74 to 1.29)†	0.88 (0.51 to 1.52)	1.34 (0.85 to 2.13)	0.85 (0.41 to 1.75)	1.91 (1.03 to 3.57)	0.84 (0.53 to 1.35)
99.0–278.5	0.74 (0.54 to 1.00)	0.78 (0.44 to 1.41)	1.18 (0.71 to 1.95)	0.86 (0.41 to 1.83)	1.52 (0.78 to 3.05)	0.40 (0.20 to 0.78)
278.6–545.2	0.92 (0.62 to 1.35)	0.85 (0.42 to 1.72)	1.21 (0.66 to 2.25)	1.31 (0.57 to 3.00)	1.08 (0.43 to 2.72)	0.90 (0.43 to 1.86)
545.3–4,361.9	1.15 (0.77 to 1.74)	1.56 (0.80 to 3.01)	1.40 (0.71 to 2.76)	1.89 (0.79 to 4.51)	0.76 (0.23 to 2.50)	0.61 (0.34 to 1.92)
p for trend	0.67	0.32	0.05	0.03	0.47	0.48

* CVD, cardiovascular disease; IHD, ischemic heart disease; TOTTEQ, toxic equivalencies of polychlorinated dibenzo-*p*-dioxins and furans.
† Numbers in parentheses, 95% confidence interval.

TABLE 7. Cancer mortality in relation to quintiles (upper quintile divided into deciles) of TCDD* and TOTTEQ* levels (ng/kg of blood fat) at the end of exposure, excluding persons from the opiate department (chemical workers only, two lowest quintiles as reference): Hamburg, Germany, 1952–1992

TCDD concentration	Cancer	TOTTEQ concentration	Cancer
0–14.4	1.0	1.19–39.5	1.0
14.5–49.2	1.20 (0.66 to 2.19)†	39.6–98.9	0.90 (0.48 to 1.67)
49.3–156.7	1.33 (0.73 to 2.40)	99.0–278.5	0.91 (0.48 to 1.73)
156.8–344.6	1.15 (0.57 to 2.30)	278.6–545.2	0.99 (0.45 to 2.13)
344.7–3,890.2	2.28 (1.14 to 4.59)	545.3–4,361.9	1.73 (0.81 to 3.66)
p for trend	<0.01	*p* for trend	0.06

* TCDD, tetrachlorodibenzo-*p*-dioxin; TOTTEQ, toxic equivalencies of polychlorinated dibenzo-*p*-dioxins and furans.
† Numbers in parentheses, 95% confidence interval.

mortality of the highest TCDD exposure increased to 2.28 (95 percent CI 1.14 to 4.59), and the test for trend was significant.

DISCUSSION

The results of analyses using an external referent group revealed trends of increasing risk for total mortality, cancer mortality, and ischemic heart diseases mortality with increasing estimated levels of TCDD and total toxic equivalencies. For cardiovascular diseases other than ischemic heart diseases and for non-cancer/noncardiovascular diseases taken together, no dose-related trend was observed. However, significantly elevated risks were observed for these outcomes in some exposure categories. Deviations from the trend for total mortality, cancer, and ischemic heart diseases occurred, especially in the lowest TCDD and total toxic equivalencies categories, thus complicating the evaluation of the analyses using only the PCDD/F-exposed cohort. This comparison showed a similar pattern of effects across exposure categories, but the effects were lower and the trends were not as

marked as in the analysis using an unexposed reference cohort.

The subanalysis of cancer mortality controlling for coexposure to dimethyl sulfate indicates that deviations from the trend may be due to exposure to other carcinogens.

Information was not available to assess possible confounding factors for ischemic heart diseases in the workplace, such as stress related to shift work or exposure to some solvents (37). However, even in the internal comparison, the highest risk estimates for cancer and ischemic heart diseases were consistently found in the highest exposure groups, and the tests for trend remained significant or of borderline significance for cancer and ischemic heart diseases. Furthermore, the relative risk for cancer mortality of 2.03 in the highest TCDD group was significant. No dose-related trend was observed for all other causes combined. This does not necessarily imply the lack of an effect of TCDD and total toxic equivalencies on other causes of death. For example, we reported an elevated standardized mortality ratio for suicide in the chemical worker cohort with respect to the German population (6).

The major strength of the present study is the availability of a quantitative measure of exposure, which allows a direct estimate of dose-response relations. The exposure indicator is based on the relation between work histories and blood or adipose tissue levels of PCDD/F from about 16 percent of the cohort. However, there are several potential sources of error and bias in this measure that must be considered. One possible source of bias is the lack of random sampling of the subgroup with PCDD/F assays. Bias in the slope of tissue TCDD regressed on the duration of employment in a particular department could arise, for example, if workers with long durations and low TCDD levels were systematically underrepresented in the validation study. In order for such bias to induce confounding between exposure and mortality outcomes, it would be necessary that any bias in the exposure measure be related to disease status (or other risk factors for early mortality). Indirect evidence that such selection factors were either not operative or were consistent over time stems from the fact that the pattern of effects of different employment durations on PCDD/F levels changed little from the analysis of the first 92 workers examined (30) to the analysis presented here for 190 workers.

A second source of uncertainty in the exposure measure follows from the fact that the estimates of PCDD/F levels at the end of exposure (when employment in a department ended) were derived from blood measurements years later. Consequently, the assumption of first-order kinetic elimination is a potential source of bias. If the kinetics are not first order, or the estimate of half-life is inaccurate or inappropriate, then estimates of tissue PCDD/F levels during exposure could be biased for workers with greater lengths of time between exposure and PCDD/F assays. The half-lives used were from our own study (31), and they are in good agreement with estimates from other studies (38–40), especially for TCDD. In order to assess the impact on results of alternative assumptions about half-lives and kinetics, we conducted some sensitivity analyses (data not shown). We did not find substantial deviations from the results presented here on relative risk estimates. The possibility of confounding due to bias in estimated exposure cannot be eliminated. However, the magnitude of the observed relative risks at higher levels of exposure could only be explained by even stronger associations between bias in measurement and mortality risks.

The relation of the different mortality outcomes to the higher chlorinated dioxins and furans was assessed by expressing the latter in terms of TCDD toxicity by toxic equivalency factors. These have been derived from animal studies addressing different toxic endpoints (carcinogenic, reproductive, immunologic, teratogenic (41)). Use of these toxic equivalency factors in the calculation of the exposure parameters in our cohort assumes that these factors reflect the toxic potency of the different congeners in humans and with regard to the endpoints under study. The similarities of the observed dose-response patterns for TCDD and total toxic equivalencies are consistent with this assumption.

The known risk factors for the different mortality outcomes under consideration could not be assessed on an individual basis in our study. Potential confounding has to be taken into consideration. With regard to smoking, we pointed out earlier that the available data on a subgroup of the study cohort indicated comparable prevalences of smoking in the two cohorts (73 percent prevalence for self-reported smokers and exsmokers among chemical workers, 76 percent prevalence among gas workers (6)). In addition, for the 480 chemical workers with known smoking history, the correlation between smoking status (ever vs. never) and estimated TCDD levels was $r = 0.065$ ($p \geq 0.10$). This small association indicates that smoking is unlikely to have seriously biased the estimate of the relation between PCDD/F exposure and mortality.

With regard to ischemic heart diseases, other established risk factors (serum lipoproteins, blood pressure, diabetes, and body mass index) could be confounders of the observed [illegible]

strongly associated with assignment to jobs with higher PCDD/F exposure. While such a job assignment process seems unlikely, there is evidence from epidemiologic findings and animal models suggesting that some risk factors for these ischemic heart diseases may be impacted by PCDD/F exposure. Such effects would constitute a causal pathway by which an impact of PCDD/F exposure on ischemic heart diseases mortality might operate. In order for the observed associations between PCDD/F exposure and mortality to be due to confounding, there would have to have been a strong selection process operating in which workers with increased mortality risk for other reasons were placed in high PCDD/F exposure jobs.

The statistical analyses were performed using an external cohort and the two lowest PCDD/F quintiles of the cohort of chemical workers as reference categories. The strength of the internal comparison is that possible differences between the study and reference groups that could have affected the mortality (socioeconomic status, medical selection at the time of entry into the plant, health care) are minimized. The internal comparison is critical in two additional respects. 1) On the one hand, the available blood levels showed that the internal reference group was not at background exposure to PCDD/F and that the potential for PCDD/F exposure misclassification was larger in the lower dose ranges, indicated by the large confidence intervals of the department-dependent exposure estimates (table 1). 2) On the other hand, this comparison could be biased by exposure to other substances, especially carcinogens or suspected carcinogens, that were associated with lower PCDD/F exposure. One such substance was dimethyl sulfate exposure in the opiate department of the plant where, if at all, low exposure to PCDD/F had occurred. As outlined in the subanalysis excluding workers from this department, the dose-response curve for cancer mortality became more pronounced. Other substances of interest might have been benzene and the different isomers of hexachlorocyclohexane. Exposures to these were highest in the hexachlorocyclohexane and lindane departments, for which low PCDD/F exposure was estimated (see table 1). The advantage of the external comparison is that the baseline category consists of a cohort with only background exposure to PCDD/F and, besides exposure to benzene in a subgroup, also to other carcinogens.

The socioeconomic status of both cohorts is comparable, and both come from the same region. There is no indication that company medical selection or health care differed between the cohorts. The standardized mortality ratio for total mortality for the reference cohort in relation to the population of the Federal Republic of Germany was 0.80 (95 percent CI 0.75 to 0.86), indicating a healthy worker effect. However, the standardized mortality ratio for all cancers combined was 0.96 (95 percent CI 0.87 to 1.06) (34). Thus, especially with respect to cancer mortality, it is reasonable to assume that the observed elevated relative risks for the chemical workers could not be attributed to unusually low mortality in the referent cohort.

Other mortality studies in the context of PCDD/F exposure have shown no consistent pattern with respect to ischemic heart diseases mortality. However, these studies have not included detailed exposure-response analyses. Zober et al. (5) observed a slight elevation of deaths due to cardiovascular diseases (ICD-9 codes 390–459). Based upon only 24 deaths, they found a standardized mortality ratio of 1.21 (90 percent CI 0.83 to 1.7). In a study with much more power, Fingerhut et al. (4) reported a standardized mortality ratio of 0.96 (95 percent CI 0.87 to 1.06) based on 393 cases. No detailed exposure-related analysis for ischemic heart diseases was reported. A study from the Netherlands (42) found eight deaths due to myocardial infarction in a group of 141 workers exposed in a TCDD accident in 1963. Seven of these workers suffered from severe chloracne. Other occupational mortality studies have shown slight nonsignificant elevated risks for arteriosclerotic heart diseases (43) or no effect (44, 45).

In the Seveso mortality study (46), an elevated standardized mortality ratio was observed for all cardiovascular diseases (standardized mortality ratio = 1.75, 95 percent CI 1.0 to 3.2) and for ischemic heart disease (standardized mortality ratio = 2.22, 95 percent CI 0.8 to 5.9) in the population of the most contaminated zone A. In light of our findings, the speculation of the authors that the increased ischemic heart diseases mortality in Seveso may have been due to the stress of the accident needs to be reconsidered.

It is difficult to draw conclusions on the reaction of the dose-response curve in the low- to mid-dose region. This difficulty arises from potential exposure to other carcinogens and potential increases in measurement errors in these groups. Future work with these data will focus on these issues. However, visual inspection indicates that both the ischemic heart diseases and cancer curves showed a sublinear form. The tests for trend were significant, indicating the presence of dose-related effects. For ischemic heart diseases mortality in the external comparison, a numerical but nonsignificant elevation in risk was observable at the lowest dose (about 100 ng/kg of total toxic equivalencies). The elevation of cancer mortality was significant or of borderline significance throughout the whole dose range. While the [illegible] heart diseases

are consistent with a threshold model, those on cancer do not suggest a threshold.

In summary, the results of this cohort study support the hypothesis of a dose-related effect of PCDD/F on cancer and ischemic heart diseases mortality. In the case of cancer, these findings refine the strong existing evidence of a carcinogenic effect of PCDD/F in humans. In the case of ischemic heart diseases, there is some evidence from animal models that TCDD may promote atherosclerosis, and this lends credibility to a causal interpretation of our findings. However, the inconsistency of findings across epidemiologic studies indicates the need for further investigation. Future morbidity studies should address this question in greater detail.

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Dow Brand Dioxin:

Dow Makes You Poison Great Things

Edited by Jack Weinberg,
Contributors include Joe Thornton, Charlie Cray and Bill Walsh
Assisted by Bonnie Rice and Katherine Schultz

-- launched a new trade group, the Chlorine Chemistry Council, to handle public relations, political lobbying, and "scientific initiatives" on all issues for the chlorine industry From its origin, the CCC was a Dow-led effort The Council's first managing director was Brad Lienhardt, a career-long Dow employee

According to Chemical and Engineering News, the CCC's estimated 1994 budget was $12 million In-kind contributions to the CCC-led effort from member companies was estimated at ten times that amount. This put the estimated 1994 resources of the CCC at over $130 million [Hirl 1994]

The CCC made its muscle apparent It published a thousand-page "scientific" report, prepared by consultants which reviewed the toxicology of a wide range of organochlorines and concluded that chlorinated organic chemicals can not be regulated as a class, and that as currently used, they are safe for health and the environment. Some consultants who helped prepare and review this report were respected academics who subsequently became vocal critics of environmental groups and agencies seeking to phase-out or restrict chlorinated chemicals

The CCC contracted with public relations firms and hired its own public relations staff In 1994, it got an opportunity to flex political muscle when the Clinton White House proposed that EPA conduct a study of the environmental and health impacts of chlorinated organic chemicals

The CCC immediately expressed "outrage" It generated, by its own estimate, a million letters to Congress CEO and other senior officials were instructed to contact a long list of representatives, cabinet members, and executive branch appointees The CCC sought to generate hysteria by mischaracterizing the proposed study as "EPA's Recommendation to Ban Chlorine " [Lienhardt 1994]

Dow wrote to all its customers and requested that they and their employees write to the President and Congress and oppose any study of chlorine [Sosville 1994] Dow told the press and its employees that EPA planned to "ban" chlorine and that Dow's Michigan division, "which employs about 3500 people, doesn't have replacement products in mind should chlorine be banned " [Henze 1994]

Dow CEO Frank Popoff mischaracterized the proposed study as "EPA is trying to ban an element on the periodic table " [Popoff 1994] CMA officials met with cabinet members and secured a "moderating statement " Ultimately, Congress and EPA failed to act on the proposed study

4 4 The Dioxin Reassessment Undermining Science at EPA

In 1994, EPA scientists released the long-awaited draft of their Dioxin Reassessment This document was prepared over the course of three years by scientists at EPA, the National Institute

of Environmental Health Sciences, and other agencies, was reviewed by numerous expert panels during the drafting processes, and was aired in pre-draft form at public hearings in several cities

The document concluded that dioxin was an extraordinarily potent environmental hormone, caused a wide variety of toxic effects, and that background exposures may already be in the range at which health effects can occur The authors of EPA's report also published the majority of their findings in peer-reviewed scientific journals and books

Dow and the CCC moved immediately to undermine EPA's alarming findings CCC organized a public relations push, and EPA public hearings in Washington on the reassessment were dominated by the CCC's hired scientific consultants The main thrust of the Dow/CCC offensive, however, centered on the EPA Science Advisory Board, which was slated to review the draft reassessment

The SAB held one meeting to receive public comment testimony consisted of a fifteen minute presentation by a single environmental group and thirteen presentations by industry and its consultants, for a total of 3 hours and 40 minutes The CCC and its consultants made several separate presentations at which EPA's conclusions were attacked in the most strident tone

More significantly, the chemical industry's influence extended to members of the SAB panel, the group given the task of drafting the SAB's review of the Dioxin Reassessment's chapters covering health risks associated with dioxin in the environment. Two individuals stand out William Greenlee, a Scientist then at Purdue University, and John Graham of the Harvard Center for Risk Analysis

Observers close to the review process have identified Greenlee and Graham as the two members of the SAB health panel who most actively and consistently challenged the validity of the dioxin health risk conclusions contained in the EPA Report Greenlee and Graham were the panel members who pressed most vigorously and effectively for an outright rejection of the risk characterization section of the report Were Greenlee and Graham truly objective reviewers?

During an SAB meeting in May, 1995, panel members were asked to disclose research grants in dioxin-related fields The transcript shows that Greenlee stated

> *I'm Bill Greenlee from Purdue University In addition to funding from NIH, I have received research grants from the American Forest Paper Association and General Electric, and I've also received gifts for research from Chemical Manufacturers Association and Dow Chemical* [ECR 1995]

The descriptive term "gifts for research" is highly unusual Why does Greenlee distinguish these from his "research grants " Records from the Purdue University School of Pharmacy and Pharmacal Sciences describe grants from Dow and CMA to Greenlee as having been awarded for a "dioxin research program" for the period July 1, 1994 through June 30, 1995 [Purdue, 1995]

These grants amounted to $45,000 from Dow and $75,000 from CMA Greenlee's "dioxin research program" also reportedly received $65,000 from the American Forest & Paper Association (AFPA) during the same period [Purdue, 1995]

In addition, Greenlee received a 1993-94 grant from the AFPA for $973,800 to study "Development of a Biological Basis for Dioxin Risk in Humans [Purdue 1994] In a private conversation with editors of the newsletter "Waste Not," Greenlee confirmed he had administered grants to study dioxin for several million additional dollars from the AFPA prior to his tenure at Purdue

AFPA is the industry organization serving as the primary representative of pulp and paper manufacturers opposing regulations and legislation to curtail dioxin emissions from mills that bleach with chlorine-based chemicals CMA (together with its subsidiary, the Chlorine-Chemistry Council) is the industry organization serving as the primary representative of the chlorine-chemistry industry on dioxin-related matters Dow Chemical is probably the world's largest root source of dioxin Greenlee's history of service to these organizations helps explain a strangely candid comment in the transcript of the SAB panel's May meeting Commenting on "very personal questions about our own biases," Greenlee said "Those of us for whom dioxin supports our family, sometimes we keep looking for problems that aren't necessarily there because it puts food on the table " [ECR]

John Graham serves as director of the Harvard Center for Risk Analysis In the month prior to the SAB meeting, Graham's Center organized a high-profile conference on drinking water and health risks, "financed by a grant from the Chlorine Chemistry Council and the Chemical Manufacturers' Association " [CCC 1995] Graham's Center has also received unrestricted grants of funds from Dow Chemical in the years 1990, 1991, 1992 & 1993. In addition, his Center has received unrestricted grants of funds from several other companies with a strong interest in the outcome of EPA's Dioxin Reassessment including CIBA-GEIGY, DuPont, GE, Georgia-Pacific, Hoechst-Celanese, ICI, Kodak, Monsanto and Olin

Individuals like Greenlee and Graham, whose careers are enhanced by their ability to raise large sums from dioxin-interested corporations should not have agreed to participate on the health panel They should have recused themselves to avoid the perception of a conflict of interest Instead, both vigorously participated in the work of the panel intervening at every occasion to challenge and downplay EPA's characterization of health risks associated with dioxin

At the time of this writing, the SAB panel's report is not yet complete (though a final draft will likely be complete by time this report is released) The likely final product will be a consensus document that makes no one happy On the one hand, scientific evidence presented by EPA linking minute levels of dioxin in the environment to potential public health injury is so strong it is unlikely efforts by panel members such as Greenlee and Graham to utterly discredit EPA conclusions will prevail On the other hand, by the nature of consensus, strong

disagreements on the panel will likely be reflected in language that muddies the EPA's conclusions and helps lay the basis for further delays in taking action.

As such, Dow and its chemical industry allies will have achieved another victory. Delay and confusion have always been primary industry goals. This is the third EPA dioxin reassessment in 10 years, and the existence of an on-going reassessment has been used as an excuse for making no decisions in the interim. Each new study has been undertaken at the urging of the chemical and paper industries.

The chemical industry made its "delay by studying" strategy clear at a CCC strategy session held in 1994. The newspaper In These Times obtained the notes of a guest at the meeting.

> *The speakers acknowledged that industry is vulnerable to being regulated because "dioxin can go in any direction" as a public relations issue. People don't have a bad idea of chlorine, but they do about dioxin. We were cautioned to "downplay the connection.*
>
> *We were also warned that chlorine customers are very concerned about chlorinated hydrocarbons that contaminate the environment and act as estrogen mimickers that disrupt the body's glandular system. We were advised to respond to questions with long-term scientific predictions -- 10 years in the future -- that cannot be verified. They said USA Today in particular cannot resist such predictions. And they advised, "If you ever come across research that is negative, just talk about the need to do more research and study the issue.* [Bleifuss 1995]

Institute for Agriculture and Trade Policy 612-379-5980 12/6/95 4:31 PM 1/

December 6, 1995

Honorable Dana Rohrabacher
House of Representatives
Washington, D.C. 20515

Dear Mr. Rohrabacher,

Regarding the December 13th hearing on EPA's dioxin reassessment by the Subcommittee on Energy and Environment, we would like you to add several key witnesses (see attached list) to the Subcommittee's current witness list.

As you know, dioxin has become a major public health and environmental threat, for which the scientific evidence, including that presented in the form of EPA's dioxin reassessment, is unassailable. For example, the review committee of the Science Advisory Board "signed off" on the issues of greatest concern to the American people. The review committee agreed with the EPA that:

• Dioxin is a probable human carcinogen.

• Dioxin harms the reproductive and immune systems and impairs normal child development at extremely low levels of exposure. Dioxin exposure is associated with endometriosis, decreased testosterone levels and sperm counts, glucose intolerance, immune system suppression, infertility, birth defects and other serious health problems.

• Dioxin is more toxic than virtually all other compounds the EPA has studied. The margin of safety between exposure and health effects is smaller for dioxin than for other chemicals.

• The American people are being exposed to dioxin through the food we eat every day. The consumption of dairy products and meat contribute over ninety percent of the average daily intake.

• Dioxin comes from human-made sources like incineration, paper and PVC manufacturing, and the production of chlorinated pesticides and other chlorinated organic compounds.

What is abundantly clear to those of us who have followed environmental health regulation over the last 20 years or so, is that if dioxin had been a product, it would have been banned years ago. However, because dioxin is an unwanted by-product of many chemical, industrial, and waste-disposal processes, doing anything meaningful about it requires taking on the huge lobbying power of those special interests. Thus, even though the pollutant is in our food, in our tissues, and in mothers' breast milk at levels at which we should anticipate effects in animals, including primates, we see still more attempts to obfuscate the need for significant action in this matter. It is highly regrettable that the legislative process has been tainted by such blatant conflicts of interest.

The Subcommittee's current list of non-governmental witnesses is composed exclusively of individuals whose scientific integrity is compromised by the funding of their work by dioxin-polluting industries such as incinerator, chemical and pulp and paper corporations.

In this light, there is no defense of a hearing on this subject that does not adequately reflect the views of the vast majority of the scientific community and individual citizens who live in communities affected by dioxin.

Surely the Subcommittee intends to present the best thinking of the scientific community on this important subject. As currently structured, this hearing would serve the narrow interests of certain corporate polluters, to the detriment of public health and science itself. Congress should not be

seen as staging "witch hunts" on behalf of its campaign financiers against the exhaustive science upon which EPA's reassessment is based.

If any hearing is to be held, it should be on the protracted and unnecessary delays that have plagued the completion of this reassessment, which was originally commissioned under the Bush Administration in 1991 and was scheduled to be completed by the fall of 1993.

In an effort to bring this hearing more into balance, we have attached a list of many qualified experts who would make excellent witnesses on this issue. We would like to discuss this list with you and/or your staff, as soon as possible.

Thank you for your most serious consideration of this matter.

Sincerely,

Rick Hind
Greenpeace
Washington, DC

Jackie Hunt Christensen
Institute for Agriculture & Trade Policy
Minneapolis, MN

Charlotte Brody
Citizens Clearinghous for Hazardous Waste
Falls Church, VA

Dr. Paul Connett
Professor of Chemistry
St. Lawrence University
Canton, NY

Terri Swearingen
Tri-State Environmental Council
Chester, WV

Alonzo Spencer
Save Our County
East Liverpool, OH

Stormy Williams
California Communities Against Toxics
Rosamond, CA

Keith Ashdown
Cancer Prevention Coalition
Chicago, IL

John Pruden
National Citizens Alliance
Ossineke, MI

Denise Lee
Anson County Citizens Against Chemical
Toxins & Underground Storage
Wadesboro, NC

Wendy Gordon
Mothers & Others for a Livable Planet
New York, NY

Frances Dunham
Citizens Against Toxic Exposure
Pensacola, FL

Peter Washburn
Natural Resources Council of Maine
Augusta, ME

Bryony Schwan
Women's Voices for the Earth
Missoula, MT

Joe Thornton
Center for Environmental Research and
Conservation, Columbia University
New York, NY

Theresa Mills
Parkridge Area Residents Take Action
Columbus, OH

Alicia Culver
Government Purchasing Project
Washington, DC

Ann Hedges
Montana Environmental Information Center
Helena, MT

Daniel Rosenburg
U.S. Public Interest Research Group
Washington, DC

Lorrie Cotterill
Groups Allied to Stop Pollution
Wilmer, TX

Nina LaBoy
South Bronx Clean Air Coalition
Bronx, NY

Jane Williams
Desert Citizens Against Pollution
Rosamond, CA

Marti Sinclair
Adans for a Clean Environment
Ada, OK

Carol Dansereau, J.D.
Washington Toxics Coalition
Seattle, WA

Joan Garrett
Lehigh Valley Coalition for a Safe Environment
Nazareth, PA

Liz Crowe
Kentucky Environmental Foundation
Berea, KY

Sue Pope
Downwinders At Risk
Midlothian, TX

Joanne Almond
Stanly Citizens Opposed to Toxic Chemicals
Albemarle, NC

Michael Gregory
Arizona Toxics Information
Bisbee, AZ

Scott Sederstrom
Great Lakes United
Ann Arbor, MI

LaNelle Anderson
Channelview Citizens Against Environmental Contamination
Channelview, TX

Kim Phillips
Midway High School Parent-Teacher Association
McGregor, TX

Ellen Connett
Editor, *Waste Not*
Canton, NY

Richard Schweiger
Community Nutrition Institute
Washington, DC

Elmer Savilla
Partners in the Environment
Mount Vernon, VA

Corinne Whitehead
Coalition for Health Concerns
Benton, KY

Barbara Mohon
Gulf Coast Environmental Defense
Gulf Breeze, FL

Craig Williams
Chemical Weapons Working Group
Berea, KY

Linda Lott
Citizens United and Aware for a Safe Environment
Midlothian, TX

Bill Freese
Huron Environmental Activist League
Alpena, MI

Greg Karras
Communities for a Better Environment
San Francisco, CA

Neil Carman, Ph.D.
Lone Star Chapter of the Sierra Club
Austin, TX

Sarah Barnard
Montanans Against Toxic Burning
Bozeman, MT

Phyllis Glaser
Mothers Organized to Stop Environmental Sins
Winona, TX

Alisa Gravitz
Co-op America
Washington, DC

Beatrice Taggart
Citizens Opposed to Polluting the Environment
Holbrook, MA 02343

Potential Witnesses for December 13th Hearing on "Scientific Integrity and Federal Policies and Mandates: Case Study 3 -- EPA's Dioxin Reassessment

Dr. Linda Birnbaum, the EPA scientist most responsible for writing "Chapter 9" of the dioxin reassessment.

Dr. Richard Clapp, Director of Center for Environment Health Studies at the Boston University School of Public Health and member of the SAB panel that recently evaluated the reassessment for the EPA.

Dr. Arnold Schecter, of the State University of New York at Binghamton and the first scientist to document dioxin in human tissue and food, on whose work the reassessment is, in part, based.

Dr. Paul Connett, Professor of Chemistry at St. Lawrence University who has worldwide experience documenting the dioxin hazards posed by waste incineration.

Dr. James Dwyer, of the University of Southern California, School of Medicine who has just coauthored an article in the America Journal of Epidemiology showing "a strong dosedependent relation between mortality due to cancer or ischemic heart diseases and exposure to polychlorinated dioxins and furans" based on a study of more than 1,100 chemical workers.

(Ret.) Admiral Elmo Zumwalt,Jr., former Chief of Naval Operations, a major participant in government efforts to study dioxin containing Agent Orange with additional expertise in selecting panels of scientists who are not funded by or agents of dioxin-producing companies.

Lois Marie Gibbs, a former resident of Love Canal, New York who has just written a book *Dying From Dioxin*, and who also heads up the Citizens Clearing House for Hazardous Waste.

If for some reason any of these people are not available on December 13th, we would be happy to recommend other equally qualified experts for this hearing.

THE WALL STREET JOURNAL WEDNESDAY, JULY 19, 1995

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Letters to the Editor

EPA's Dioxin Review Is Science, Not Policy

I am concerned about the portrayal of EPA science in Kathryn E. Kelly's June 29 editorial-page piece "Cleaning Up EPA's Dioxin Mess."

The author's inaccurate version of what the EPA's Science Advisory Board has said about the agency's draft dioxin reassessment misses the point. The EPA welcomes the in-depth review of its dioxin report as part of a continuing effort to involve the full range of scientific opinion in reaching its conclusions. However, in my view, it is premature for the author to make such harsh indictments when the board has not yet completed a draft of its report.

In criticizing the reassessment as faulty policy, Ms. Kelly again misses the point. This is a scientific assessment, not a regulatory approach. She falls victim to the same fault she attributes to the agency: confusing science with regulatory decisions.

Contrary to the author's assertion, research done at the EPA is scientifically credible, it is subjected to independent peer review and it is independent of regulatory objectives. Ms. Kelly suggests that because the EPA has a vested interest in regulating dioxin, it has compromised its scientific integrity. First, she is wrong to say that "much of EPA's flawed position on dioxins has been based on internal research." While the EPA has been an international leader in certain areas of dioxin research, the 2,600-page analysis included peer-reviewed literature from around the world, most of which was not performed by the EPA. Second, any interested observer of EPA science would know that the peer review process has been the focus of intense scrutiny internally at the EPA for the past several years, and that the agency is strongly committed to using peer-reviewed science, both its own and from others, in its analyses. Third, the dioxin assessment has been exemplary of an open and participatory scientific process, involving hundreds of scientists from outside of the agency. It has received praise from many quarters in that regard: Is it to be inferred that all these scientists share the same bias and regulatory objectives?

I believe the steps we have taken to ensure full participation by the scientific community, independent peer review of our work and open and continuing public involvement in the process represent the best way of doing risk assessments. These actions will ensure that the EPA's decisions to protect public health and the environment are based on sound science.

ROBERT J. HUGGETT, Ph.D.
Assistant Administrator
for Research and Development
Environmental Protection Agency

SAB Chair Response to Wall Street Journal Article on Dioxin

July 6, 1995

Mr. Ned Crabb
Letters to the Editor
Wall Street Journal
200 Liberty Street
New York, NY 10281

Dear Mr. Crabb:

As Chair of the EPA Science Advisory Board (SAB) review committee for EPA's Dioxin Reassessment Review, I was disappointed at the rush-to-judgment article that appeared in the Wall Street Journal of June 29 under the byline of Kathryn E. Kelly and headed "Cleaning up EPA's Dioxin Mess." Ms. Kelly's characterization of the SAB panel's assessment of the EPA document can only represent her own speculation and preconceptions, since the SAB Committee has not yet come to final consensus judgments. Also, her characterization of comments by individual members of the SAB panel are not consistent with those made during the panel's deliberations.

While many of the oral comments of members of the SAB Committee at the meeting and many of their written comments in the draft report, currently in preparation, are critical of the EPA's reassessment document, many others were quite complimentary of EPA's efforts to make a full and balanced report. Furthermore, much of the new and valuable infomation has come from EPA's own research. EPA should be commended for the well-targeted research that it has published in the peer-reviewed scientific literature on this important topic, and Ms. Kelly's mischaracterization of this research as policy or politically driven is misguided and misleading.

The solution to the dilemmas arising from costly regulations in the absence of adequate scientific knowledge lies in more research of the kind Ms. Kelly attacts, not in less.

Finally, if EPA really wanted to rush to regulate Dioxin sources in the environment, it would not have bared its soul (and warts) before an SAB review panel in open session. Based upon my past experience in comparable reviews of documents on environmental tobacco smoke and criteria air pollutants, EPA will carefully consider the forthcoming SAB review commentary and prepare an improved dioxin reassessment that will provide it with a firmer basis for any regulatory decisions that it may eventually make.

Very truly yours,

/signed/
Morton Lippmann, Ph.D.
Professor
New York University Medical Center

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MAR 27 1996

OFFICE OF CONGRESSIONAL
AND LEGISLATIVE AFFAIRS

Honorable Dana Rohrabacher
Chairman
Subcommittee on Energy
and Environment
Committee on Science
House of Representatives
Washington, D. C. 20515-6301

Dear Mr. Chairman:

This is in response to your letter of February 14, 1996 to Dr. William H. Farland, Director of our National Center for Environmental Assessment, containing 15 questions concerning the Agency's mercury study. The questions appear to be based on the external review draft of the Mercury Study Report to the Congress made available in December 1994.

The Report is now undergoing extensive interagency review under the auspices of the Office of Management and Budget. It is expected to be finalized in time to be made public on or about April 15, 1996, as required by court order. The comments of all interested Executive Branch agencies are being addressed and the Report being revised. Until this process is complete and the Report is final, we will not be in a position to respond to your questions. We will do so upon completion of the Report.

In the meantime, if we can assist you in any way, including a briefing on the Report development process, we would be glad to do so.

Sincerely,

Lynne M. Ross

Lynne M. Ross
Director, Legislative Division

U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON SCIENCE
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February 14, 1996

Dr William H Farland
Director for the National Center for Environmental Assessment
Office of Research and Development
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460-1101

Dear Dr Farland

Thank you for your excellent testimony before the Subcommittee on Energy and Environment on December 13, 1995 regarding EPA's reassessment of dioxin

Enclosed are some additional questions submitted by Congresswoman Barbara Cubin. I would appreciate receiving your responses by Wednesday, February 28, 1996. The information will be included as part of the official printed record of the December 13 hearing. Please forward this information to the Subcommittee office, B-374 Rayburn House Office Building, Washington, DC 20515 to the attention of Ms Jennifer Disharoon, Staff Assistant.

Again, thank you for your valuable contribution to the hearing.

Cordially,

Dana Rohrabacher
Chairman
Energy and Environment Subcommittee

DR jld

Enclosure

Questions to William H. Farland,
Director of Health and Environment Assessment
US EPA

During your testimony on December 13, you indicated certain procedures would be followed to assure that future studies submitted to Congress by EPA would be based on a process that would result in an "open, participatory environmental health assessment."

The following questions concerning the EPA'a mercury report to Congress are submitted in view of this commitment.

1.) The EPA computer air model used to predict the fate and transport of mercury in the atmosphere results in predictions that greatly overly exaggerate mercury deposited in the environment. EPA model results are high by a factor of 10 to 100 based on actual field observations. For example, EPA's predicted high-end range for mercury in fish due to atmospheric mercury is 14 times higher than the highest levels actually found in fish (26 ug/g versus 1.8 ug/g). In fact, levels of mercury in fish actually swimming in a concentrated discharge of mercury waste were lower than the levels of mercury predicted by EPA's model for fish generally.

1A.) How has EPA resolved the problems with these flawed computer models?

1B.) How has EPA validated the fate and transport models for mercury emissions?

2.) EPA's model is based on non-peer reviewed, multi-media modeling, with seemingly no validation from field data. Industry would not be permitted to use the EPA model in submitting applications for permitting facilities, yet EPA uses the model indiscriminately. EPA recently changed the air quality models from the model (ISC3). The ISC3 model continues to have some of the same problems in overly exaggerating deposition of mercury as COMPDEP.

How has EPA resolved the problems regarding wet and dry deposition so that the computer model does not overly exaggerate mercury deposition concentrations?

3.) There is a significant body of information on the actual mercury content of fish, within EPA and at various agencies. It should be relatively easy task for EPA to validate its models by comparing the model results to real life. EPA itself has acknowledge that the models used by the Agency overly predict concentrations actually found in fish swimming near sources of atmospheric mercury.

Given EPA's admission that the models used are inaccurate, what steps are being taken to validate each model and each assumption used in the models?

4.) EPA's modeling of impacts of deposited mercury on surface water runoff carrying this mercury into lakes and streams does not seem to incorporate even the latest models used by EPA's own water quality staff.

What are the models used by the EPA's water quality staff and how do they differ from the models used in the Mercury Reports to Congress. Most important, why do they differ?

5.) Do the FDA, NIEHS and the EPA agree on an ADI or RFD for methyl mercury where exposure is from consumption of ocean fish?

6.) A respected scientist, Dennis Crump analyzed the data from the Iraqi incident used in the mercury report and concluded that it supported an RFD about eight times higher than that determined by EPA. How do you account for such a significant difference in interpretation of the same data?

7.) EPA's projection of fish consumption rates is based on a three day dietary study which shows about 30 percent of the population eating fish in the three day span in which almost all data points represents a single meal.

8.) What assumptions are made to extrapolate this information to a daily input over a long enough period to be relevant when comparing it to an RFD which by definition pertains to lifetime exposure?

9.) The NIEHS Report on Mercury (January, 1993) recommends a study is needed to confirm the mercury developmental toxicity threshold predicted from the Iraq studies. NIEHS recommends the study confirm the mercury threshold for the U.S. population (or an analogous population) the consumes methylmercury in fish. Does EPA agree with this recommendation and, if not, why not? Do the Seychelles Island studies fulfill the NIEHS recommendation?

10.) EPA has based its assessment of the human and environmental effects of mercury on short term, massive exposures to mercury or methylmercury. How are studies such as the Seychelles Islands study of chronic, long term exposures to low levels of methylmercury through fish consumption consideration by the Agency?

11.) EPA previously calculated reference doses for methylmercury chronic toxicity and for methylmercury developmental toxicity. These references doses are associated with woman of reproductive age and children and adults (other than woman of reproductive age). Does EPA intend to continue treating methylmercury toxicity in this way? If not, why not?

12.) The draft Mercury Report to Congress presents only one calculated reference dose that is applied to the general U.S. population as well as sub-populations of potential special concern. This represents a change from previous EPA documents that present two very different reference doses. How is this apparent change in assessing methylmercury toxicity justified?

13.) In the June, 1994 EPA "Guidance for Assessing Chemical Contaminant Data for Use in Fish Advisories - Volume II Risk Assessment and Fish Consumption Limits" EPA states:

"Although these are numerous developmental toxicity studies available, the doseresponse results are not consistent due, in part, to the variety of endpoints which

have been evaluated. Additional studies are needed to identify a NOAEL based upon sensitive developmental toxicity endpoints."

What new studies did EPA identify in 1994 or 1995 that overcame the limitations of previous studies to allow the determination of a new NOAEL and reference dose? Why were these studies better than the previous work used in assessing methylmercury toxicity?

14.) The 1993 NIEHS Report of Mercury points our problems in making accurate estimates of United States fish consumption with available sources of fish consumption data giving inconsistent estimates. How did EPA estimate fish consumption by the general U.S. population and special sub-populations? How were the problems identified by NIEHS overcome? How do the estimates of fish consumption used by EPA for the Mercury Report to Congress compare with other estimates if fish consumption?

15.) Preliminary reports from the Seychelles Islands study indicated that there were no adverse health effects found relative to the maternal hair mercury levels that were found. how does this finding compare with the conclusions reached by EPA in the draft Mercury Report to Congress? How will EPA determine if the Seychelles Island and Faroe Islands studies justify a change in the conclusions reached in the draft Mercury Report to Congress?

MIKE DOYLE
18TH DISTRICT, PENNSYLVANIA

COMMITTEE ON SCIENCE
SUBCOMMITTEES
ENERGY AND ENVIRONMENT
BASIC RESEARCH

COMMITTEE ON
VETERANS' AFFAIRS
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December 11, 1995

Mr. Paul Sutton
Chief, Homeless Veterans' Housing Programs
Division of Veterans' Programs
101 Eggerts Crossing Road
CN 340
Trenton, New Jersey 08625-0340

Dear Mr. Sutton:

I understand that you have been in contact with the Democratic staff of the House Committee on Science with regard to the December 13 hearing on the U.S. Environmental Protection Agency's (EPA) Dioxin Reassessment, and that you intend to submit testimony on behalf of the Vietnam Veterans of America (VVA).

As the only Member of Congress to serve on both the Committee on Science and the Committee on Veterans' Affairs, I am especially concerned as to how this issue impacts our nation's veterans. I am anxious for the Science Committee to hear from the veterans' community in assessing the dioxin issue, and am hopeful that Admiral E. M. Zumwalt, Jr. will appear at the December 13 hearing on behalf of the Agent Orange Coordinating Council. Knowing of your expertise and experience in this area, I think the Science Committee would benefit from your input as well. In that regard, there are some points pertaining to the Dioxin Reassessment that I hope you would be able to address in your testimony.

The VVA's interest in the relationship between Agent Orange and dioxin exposure with the health effects experienced by those who served in Vietnam is clearly understood and widely recognized by Members of Congress. I am confident that a majority of Members are supportive of both continued research on the health effects of Agent Orange exposure, and compensation for illnesses resulting from it. However, I think that there may exist some confusion about whether VVA and the Agent Orange Coordinating Council have an interest in the contemporary scientific and regulatory issues associated with dioxin. In order to clarify this issue, please respond as to whether your organization is involved in issues relating to dioxin exposure through incineration, pulp and paper production, and other industrial activities.

I am aware that the VVA has been an advocate for research into the short-term and long-term health effects of Agent Orange exposure. Are there areas of research related to dioxin that VVA feels are important in understanding the contemporary issues associated with dioxin? If there are, how do you feel that the results of these studies were adequately addressed and incorporated into EPA's recent dioxin reassessment effort?

If you can provide a response prior to the start of business on December 13, I would be pleased to present it at the hearing for inclusion in the official record of the hearing. The fax number for my Washington office is (202) 225-3084.

I thank you in advance for your consideration and wish you and your family a happy holiday season.

Sincerely,

Mike Doyle

Mike Doyle
Member of Congress

MD:pmc

Vietnam Veterans of America, Inc.
1224 M Street, NW, Washington, DC 20005-5183
Telephone (202) 628-2700 • General Fax (202) 628-5880 • Advocacy Fax (202) 628-6997 • Finance Fax (202) 628-5881
A Not-For-Profit Veterans Service Organization Chartered by the United States Congress
"VVA, At Work in Your Community"

12 December 1995

SENT VIA FAX TO: (202) 225-3084

The Honorable Mike Doyle, Member of Congress
United States House of Representatives
1218 Longworth Building
Washington, D. C. 20515-3818

Re: Your letter of 11 December 1995;
concerning: Hearings - EPA Reassessment of Dioxin

Dear Mr. Doyle:

Thank you for your letter and interest in VVA's position relative to contemporary scientific and regulatory issues associated with dioxin exposure. Let me assure you that VVA's position is that these issues are of great concern to our membership and the leadership of VVA because of numerous environmental hazards existent in American society today. Our membership and the representatives of the National Agent Orange Coordinating Council, on which I sit as a representative for VVA, are unanimous in opposing any dilution of the draft reassessment of dioxin that has been circulated by EPA over the past two (2) years.

VVA has been actively involved in contemporary scientific and regulatory issues such as opposition to the construction of municipal incinerators, incineration of dioxin contaminated residues at Jacksonville, Arkansas, advocating for chlorine-free paper and has been an active participant in the Citizen's Conferences on Dioxin. The third such conference will convene in Baton Rouge, Louisiana in March 1996.

At our Seventh National Convention this past August, VVA created an Environmental Hazards Subcommittee to address these contemporary matters. As an attachment, I am including copies of Resolutions enacted at that convention which serve as policy statements for VVA on this issue.

Areas of research in which VVA believes resources should be directed include dioxin disposal methods and manufacture of alternatives to dioxin that will alleviate the danger of exposure to living humans and to those as yet unborn to these toxic substances, thereby significantly reducing future birth defects commonly associated with the parent's exposure to dioxin. From the documents provided by EPA, it does not appear that attention

was paid to this sort of research, much of which has been carried out over the past 15 - 20 years, both by industry and government.

Thank you for your interest in this issue and for asking for our perspective on this matter which should be of paramount concern to all Americans, veteran and non-veteran alike.

Our best wishes to you and yours in this Holiday Season.

Sincerely,

Paul L. Sutton, LM 1351, Vice-Chair
National Agent Orange/Dioxin Committee

:PLS

Attachments

cc: George Claxton, Chairman
Catherine M. Greene, Vice-Chair
Mary J. Schoelen, National Office Staff Liaison

DIOXIN DISPOSAL METHODS

AO-6-95

Issue:

Disposal and storage of dioxin-contaminated materials and sediments can have a direct health impact on all citizens of this country.

Background:

Ocean dumping of contaminated materials can directly impact on the food chain, leading to ingestion of dioxin-laced fish, fowl, etc. In addition, unrestricted disposal of dioxin-contaminated materials in landfills can affect ground water reservoirs and aquifers. Incineration of these materials may result in release into the atmosphere of potentially hazardous substances. Proper and safe disposal must be used in dealing with dioxins, VVA must remain knowledgeable about sediments and related factors and support necessary research to guarantee minimal health risks to the community.

This resolution reaffirms and updates Resolution AO-9-93.

Position:

Vietnam Veterans of America, Inc., at national convention in Houston, Texas, August 15-20, 1995, opposes ocean dumping of dioxin-contaminated materials and calls for immediate termination of this practice. VVA supports research on existing methods of disposal or storage of dioxin-contaminated sediments and stands ready to work with all concerned scientific and ecological groups to ensure proper disposal or storage of these contaminated sediments.

KOREAN VETERANS AGENT ORANGE/DIOXIN HEALTH CARE AND COMPENSATION

AO-7-95

Issue:

American veterans were exposed to Agent Orange/dioxin while serving in the Republic of Korea and no action has been taken by the U.S. government.

Background:

Veterans who served in Korea still feel the effects of exposure such as cancers, unexplained illnesses, and birth defects in their offspring. The U.S. government has never credibly dealt with the Agent Orange/dioxin issue for any veterans. American Korean veterans were not involved with the Agent Orange Product Liability lawsuit, know as MDL 381, and plaintiff veterans did not agree with the settlement.

This resolution reaffirms Resolution AO-11-93.

Position:

Vietnam Veterans of America, Inc., at national convention in Houston, Texas, August 15-20, 1995, urges all chapters, state councils, and the national leadership of VVA to apply pressure to all branches of government for research and compensation for any American veterans exposed to Agent Orange/dioxin while serving in the Republic of Korea, based upon presumptive exposure.

CHILDREN'S HEALTH CARE

AO-8-95

Issue:

There is no health care or compensation provided to veterans' children and future generations who have birth defects, deficiencies, or other disabilities resulting from their parents' exposure to Agent Orange/dioxin and other toxic chemicals while in military service.

Background:

While the health-care and compensation needs of some veterans affected by exposure to Agent Orange/dioxin are being met by the Department of Veterans Affairs (DVA) and through implementation of P.L. 102-04, services for veterans' children born with defects or learning disabilities associated with their parents' exposure to such chemicals have been ignored by all segments of the government.

This resolution reaffirms and updates Resolution AO-3-93.

Position:

Vietnam Veterans of America, Inc., at national convention in Houston, Texas, August 15-20, 1995, supports a comprehensive health-care and special-needs program to assist Vietnam veterans' children and subsequent generations who have birth defects, deficiencies, or disabilities reasonably associated with parental exposure to Agent Orange/dioxin and other toxic chemicals while in military service.

AGENT ORANGE/DIOXIN NETWORK

AO-9-95

Issue:

Although Vietnam veterans have information available to them on Agent Orange/dioxin, they lack the immediate help and support that could be achieved through a veterans Agent Orange/dioxin network. We need more expansion and development of the network because there is a strong belief that the National Academy of Sciences will not be fair in their review.

Background:

Vietnam veterans and their families are frustrated over the lack of immediate information on Agent Orange/dioxin. The DVA has not cooperated in the dissemination of accurate information. Veterans and their families need to know that there is immediate help and information for this intensely human problem. This includes the personal support that affected veterans can receive from other veterans.

The National Academy of Sciences still may have people on the review panel who are alleged to have apparent conflicts of interest. Existing dioxin research groups will be able to unite and exchange information.

This resolution reaffirms and updates Resolution AO-8-93.

Position:

Vietnam Veterans of America, Inc., at national convention in Houston, Texas, August 15-20, 1995, directs that the national Agent Orange/Dioxin Committee under the direction of the national Agent Orange/Dioxin Committee chair, shall:

1. Hold an annual Agent Orange/dioxin symposium which chapter and state council Agent Orange/Dioxin Committee chairpersons and any other interested parties may attend, for the purpose of:

a. continuing the development of national programs of direct and/or referral services;

b. continuing and enhancing an interstate and intrastate networking model of information and support services; and

c. continuing the development and implementation of questionnaires for the purpose of recording and measuring the past and current health status of VVA members, their sponses, their children, and their grandchildren.

2. Require the national board of directors to maintain budget allocations for the aforementioned activities, as needed and appropriate.

3. Actively promote and expand the Agent Orange/dioxin network.

PAPERMAKING MANUFACTURING PROCESSES

AO-10-95

Issue:

Promoting the elimination of dioxins introduced into the environment from papermaking manufacturing processes should be an objective of Vietnam Veterans of America, Inc.

Background:

The use of chlorine in the papermaking industry's bleaching processes has been proven to create dioxins which are released into the environment. In recent years, concerned with their role and their responsibility to help protect the environment, a segment of the papermaking industry has worked to develop and market "chlorine-free" paper. The term "chlorine-free" is applicable to two different processes. Most widespread is the process called "elemental chlorine-free" paper which does use chlorine in the process, but does not contribute to dioxins as a by-product. Today, "elemental chlorine-free" paper comprises about 60 - 70% of the print paper market. A small but growing segment of the industry has gone one step further. It has developed and markets a "total chlorine-free" paper which is totally free of chlorine in the manufacturing process. "Total chlorine-free" paper now makes up less than 1% of the

print paper market. Both types of "chlorine-free" paper are available and cost about 10 - 25% more than paper that is not "chlorine-free."

Position:

Vietnam Veterans of America, Inc., at national convention in Houston, Texas, August 15-20, 1995, commends those segments of the papermaking industry who are engaged in research and development of alternative manufacturing processes to eliminate the further introduction of dioxins into the environment, especially those papermakers who have gone "the extra mile" in developing and manufacturing "total chlorine-free" paper; and, in support of attaining a dioxin free environment, VVA shall take all necessary measures to maximize the use of paper products utilized and consumed by VVA that are manufactured using the "chlorine-free" processes and VVA encourages its State Councils and Chapters to do likewise.

BAN THE MANUFACTURING, SALE, AND USE OF 2,4-D

AO-11-95

Issue:

For at least 50 years the Department of Defense has intentionally exposed military personnel to potentially dangerous substances, often in secret. During the war in Vietnam, when herbicides were used to defoliate dense jungle, our military personnel were not aware of the toxicity of the chemicals used.

As a result of exposure to 2,4-D in Vietnam, veterans are being diagnosed 20 years later with rare cancers, sarcomas, immune deficiencies and Central Nervous System disorders. Children of exposed veterans are born with learning disabilities, birth defects and deficiencies.

Today, herbicide 2,4-D is being used for weed control across the United States; at National Cemeteries, school yards, golf courses and hospitals. It is used by utility companies, the Department of Transportation and railroads. Additionally, 2,4-D is being used by farmers which in turn is contaminating food crops, cattle, pigs, chickens, etc. In addition, 2,4-D is being used to eliminate the growth of plant life in our lakes, thereby contaminating our freshwater and saltwater fish.

To date, approximately 240,000 veterans have died from diseases caused by exposure to Agent Orange/Dioxin and the number climbs every day. The continued use of 2,4-D today further exposes our families and children to the same chemical our veterans were exposed to in Vietnam. This exposure jeopardizes the health of our families, children and future generations, making them susceptible to the same diseases our veterans are dying from.

Background:

Vietnam Veterans are acutely aware of the deadly consequences of exposure to 2,4-D. Health and Welfare Canada and the United States Environmental Protection Agency have identified at least four different isomers of dioxin as contaminants in 2,4-D. These dioxins include the 2,3,7,8-TCDD isomer, which is the most deadly poison known to man.

Dioxin is contaminating the food chain of Vietnam veterans and compromising the immune systems of their children. Even more seriously, 2,4-D is being used at National Cemeteries, which shows the government's insensitivity to victims that have died of dioxin related cancers.

Position:

Vietnam Veterans of America, Inc., at national convention in Houston Texas, August 15-20, 1995, will seek legislation and administrative action to help ban the manufacture, sale and use of 2,4-D worldwide.

1. VVA will take all steps necessary to promote legislation to carry out this action.

2. VVA encourages it's membership through chapters and state councils to work with representatives and state legislators to obtain their support to help ban the manufacture, sale and use of 2,4-D worldwide.

~~MEDICAL EQUIPMENT AND SUPPLIES FOR VIETNAM HOSPITALS~~

~~AO-12-95~~

~~Issue:~~

~~There exists a great need for modern medical equipment and supplies at all levels of the Vietnamese health care system.~~

~~Background:~~

~~Medical technology in the United States is in a rapid state of change and growth. Whenever new technology is introduced into a hospital, many times older technology is exchanged for newer. This older technology is of no real value to the company since no United States hospital would probably accept it. The equipment or supplies would be either scraped or donated to another country. This technology may be outdated in our health care system, but it would probably be ten to twenty years ahead of that available in Vietnam.~~

~~Position:~~

~~Vietnam Veterans of America, Inc., at national convention in Houston, Texas August 15-20, 1995, urges all chapter, state council and national leadership to survey medical manufacturing companies and respective health facilities for excess or out dated equipment and/or supplies that could be transferred to Vietnam.~~

~~U.S. TREATMENT FOR VIETNAMESE BIRTH DEFECT CHILDREN~~

~~AO-13-95~~

~~Issue:~~

~~With the limited health care resources in Vietnam, many newer techniques are not available for treating the physical deformities of Vietnamese children.~~

Background:

~~Every year hundreds of nurses and surgeons in the United States travel to other countries to perform surgeries that are not available within that country's health care system. Some of the more difficult cases are brought to the United States for more extensive treatment, surgery, and rehabilitation.~~

U.S. HOUSE OF REPRESENTATIVES

COMMITTEE ON SCIENCE

SUITE 2320 RAYBURN HOUSE OFFICE BUILDING
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February 16, 1996

Dr. Donald G. Barnes
Science Advisory Board
U.S. Environmental Protection Agency
401 M St , S W.
1145 West Tower
Washington, DC 20460

Dear Dr. Barnes:

On December 13, 1995, the Energy and Environment Subcommittee of the Committee on Science held a hearing on EPA's Dioxin Reassessment Report During that hearing, Admiral Zumwalt asserted that several members of the Science Advisory Board's dioxin reassessment review committee may have had a conflict of interest because they or their organizations received research funds from industry sources with an economic interest in the outcome of dioxin regulations

To assist the Members in evaluating these allegations, I request that you provide responses to the following items by February 23, 1996:

1) Please describe the general process by which individuals are selected to serve as SAB Members, consultants, or federal experts on specific scientific review panels such as the dioxin review. In particular, please describe the policy of the SAB with respect to participation in scientific reviews by individuals who may have financial or other conflicts of interest, and the process by which such potential conflicts of interest are identified and evaluated. Please provide copies of any written guidelines or procedures which the SAB may have regarding such policies and processes. Are individuals being considered for appointment to specific scientific review panels required to disclose whether they have any financial or other ties to industries or other special interest groups that have an economic or other interest in the outcome of the subject under review? Under what circumstances are individuals appointed to serve on special review panels if they could be considered to have such a conflict of interest?

Have Science Advisory Board Members ever recused themselves from participation in a specific review due to a real or perceived conflict of interest?

2) Please provide copies of any written materials relating to the review of potential conflicts of interest of any individuals appointed to, or considered for appointment to, the ad hoc Dioxin Reassessment Review Committee, including any disclosure statements provided by such individuals.

3) How does the Science Advisory Board ensure that its review is truly independent of the EPA office that prepared the matter under review? Are appointments to specific scientific review committees made solely within the SAB? What role or influence, if any, do EPA personnel outside of the SAB have in such appointments? Did EPA personnel outside of the Science Advisory Board have any role or influence in making appointments to the ad hoc Dioxin Reassessment Review Committee?

If you have any questions regarding this request, please call either Mr. Michael Rodemeyer (225-6375) or Dr. Jean Fruci at 225-8115. I appreciate your assistance in providing this information.

Sincerely,

George E. Brown, Jr.

George E. Brown, Jr.
Ranking Minority Member

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

February 23, 1996

Congressman George Brown
Committee on Science
House of Representatives
Washington, DC 20515-6301

Dear Congressman Brown:

I am writing in response to your February 16, 1996 letter asking for specific information regarding membership on the Science Advisory Board (SAB).

I recognize the important role that you have played in the creation and growth of the SAB over the years and appreciate your interest in making a good institution even better in the future.

As background I have included the following:

1. A brochure containing an overview of the Board's current structure and function (Attachment 1) and
2. A copy of the most recent Annual Report of the SAB Staff that provides more detailed information of membership on the Board and its practices (Attachment 2).

I have divided your three questions into smaller parts and have replied to them below.

Q1a. "Please describe the general process by which individuals are selected to serve as SAB members, consultants, or federal experts on specific scientific review panels, such as the dioxin review."

A1aa: A succinct description of Members, Consultants and Federal Experts is found in "Types of Affiliation with the SAB", Appendix B2, FY94 Annual Staff Report, EPA-EC-95-001, p. B-10, October, 1994. [Attachment 2]

In short, SAB Members are non-government scientists who

1. Are qualified by education, training and experience to evaluate scientific and technical information on matters referred to the Board and
2. Are appointed by the Administrator to serve two-year terms on the Board, working through one or more of the 11 Committees of the Board.

SAB Consultants are similarly competent individuals who are appointed by the SAB Staff Director to a one-year term and are generally called upon to augment particular review panels when additional, specific expertise is needed.

Federal Experts are Federal (other than EPA) employees who are invited by the SAB Staff Director to participate in particular SAB reviews meetings because of their peculiar experience and expertise.

A1ab: Information on the selection process for SAB Members and Consultants is found in the following

1) "Guidelines for Service on the Science Advisory Board" Appendix B1, FY94 Annual Staff Report, EPA-EC-95-001, pp. B-2 thru B-9, October, 1994 [Attachment 2]
2) "Selection of Consultants for Science Advisory Board", draft operations manual for SAB staff, January, 1995. [Attachment 3]
3) "SAB Membership Search/Selection Process", draft document being prepared for consideration by the Membership Search Subcommittee of the SAB Executive Committee, February 18, 1996 [Attachment 4]

In short, the Membership search and selection process is continually open so that nominations are accepted throughout the year. The process involves input from

a) The SAB Staff
   The SAB Staff utilize formal and informal contacts inside and outside the Agency to generate the names of strong candidates.
b) The public
   Suggestions from the public result from a generally biannual request for nominations

that is published in the Federal Register, unsolicited nominations throughout the year, and/or specific inquiries to specific groups.

c) The Agency

Agency personnel, who have often been working a particular technical issue for many months or even years, are usually aware of most of the specialists in that field and make suggestions to the SAB Staff. The SAB Staff is aware that such Agency suggestions may reflect an inadvertent bias towards individuals who are favorably disposed toward the Agency's project. Therefore, these recommendations are examined with particular care, with an emphasis on assuring a balance of points of view on the Committee.

d) The Board

Current Members of the Board provide suggestions for candidates, based upon their professional knowledge and contacts. The Executive Committee has also established a Membership Search Subcommittee, whose responsibilities have included taking a global view of the list of candidates likely to be submitted to the Administrator, checking for diversity in terms of gender, "address" (e.g., academic, environmental community, industry, etc.), minority status, and geography.

Historically, the selection process has consisted of the SAB Staff Director's presenting the Deputy Administrator with at least two names for every open slot on the Board's roster. In most cases, the Staff Director has recommended one of the two names and has included a justification for the recommendation. The final selection decisions are made by the Deputy Administrator.

Selection of Consultants and Federal Experts is a similar process, except that the appointments are made by the Staff Director, generally acting on recommendations from the Staff and the Panel Chair. The Staff and Panel Chair are aware of both the particular technical needs for a thorough, credible review and the need for balance and objectivity in the Panel itself.

NOTE: In the case of the dioxin reassessment, I recused myself from the traditional role of the Staff Director, due to my long history in working on Agency dioxin issues over the past 15 years. By

prearrangement, those Staff Director responsibilities were pass on to the Deputy Staff Director, Mr. A. Robert Flaak. Mr. Samuel Rondberg was the Designated Federal Official who carried out most of the Staff responsibilities for the review.

Q1b: "In particular, please describe the policy of the SAB with respect to participation in scientific reviews by individuals who may have financial or other conflicts of interest, and the process by which such potential conflicts of interest are identified and evaluated. Please provide copies of any written guidelines or procedures which the SAB may have regarding such policies and processes."

A1b: Regarding conflict of interest, under 18 U.S.C. Section 208(a), Federal employees, including "special government employees" that serve on the Science Advisory Board, are barred from participating in any "particular matter" which affects their employers' financial interests. As defined in the Standards of Ethical Conduct for Employees of the Executive Branch, "The term particular matter encompasses only matters that involve deliberation, decisions, or action that is focused upon the interests of specific persons or a discrete and identifiable class of persons."

Generally, the SAB doesn't deal with particular matters and, specifically, its consideration of dioxin is not a particular matter because dioxin is widespread in the environment and because the Agency's reassessment was aimed at dioxin wherever it is found and from whatever sources it might come--from food to incinerators, from volcanos to pulp and paper, from human milk to chemical companies, etc.

Under 19 U.S.C. Section 208(b)(3) agencies are authorized to waive the 208 (a) restriction where "the need for the individual's services outweighs the potential for a conflict of interest [COI] created by the financial interest involved."

Such waivers are often granted to SAB Panelists in cases in which the Board is making recommendations on general research directions (but not on specific grants and contracts, which would be "particular matters"), which could conceivably affect the financial interests of the Panelists' employer. For example, a university professor's recommendations to the Agency on research could affect the number and size of grants that the Agency supports in a given area. That research area

could be the professor's own or an area of research of some other professor at the same university. In the latter case, the professor could be totally ignorant of the fact, but it would still constitute a conflict. In such cases of research recommendations, the Agency generally issues a waiver; otherwise, the Agency would be excluding itself from the advice and insights of some of the most knowledgeable researchers in a given field.

As a part of the process of assessing whether a legal COI exists or not, each member of an SAB Panel (i.e, Members and Consultants) must submit a Confidential Financial Disclosure Report (SF-450) (Attachment 5). The information includes data on assets and income, liabilities, outside positions, agreements and arrangements, and gifts and travel reimbursements for the individual and members of his/her immediate family. The completed form is reviewed by SAB Staff, with legal counsel as needed, prior to the public review meeting and a judgment is made about whether there is a conflict-of-interest or not. By law, EPA cannot make this information available to the public.

The Board is also concerned about appearance of conflicts of interest. To address this concern, it has become the practice to begin SAB public meetings with a period of voluntary disclosure. During the disclosure period, which was adapted from a practice used in National Research Council panels, SAB Panel members may share with one another and with the public information that will help others understand "where they are coming from" on the issues. The audience is free to use this information in evaluating the individual's comments on the subjects under discussion. The following factors are generally addressed during the disclosure:

a. Research conducted on the matter.
b. Previous pronouncements (e.g., court testimony) made on the matter.
c. Interests of employer in the matter.
d. A general description of any other financial interests in the matter. (Note that none of the financial interests would constitute a legal conflict-of-interest or else the person would not be on the Panel--unless a waiver had been granted.)
e. Other links; e.g., research grants from parties--including EPA--that would be affected by the matter.

Recently, the Membership Search Subcommittee of the SAB Executive Committee has discussed approaches for improving the disclosure process. The Subcommittee will report on their discussions at the public Executive Committee on Feb. 28.

More detailed information about the disclosure practice can be found in

1) "Guidelines for Public Disclosure at SAB Meetings", Attachment to Appendix B1, FY95 Annual Staff Report, EPA-EC-95-001, p. B-8 thru B-9, October, 1994 [Attachment 2]
2) "Policy for Public Disclosure at SAB Meetings" and the attached "Mock Disclosure: How to Implement the Policy of Public Disclosure at SAB Meetings", Latest revision: August 4, 1995. [Attachment 6]

Q1c: "Are individuals [who are] being considered for appointment to specific scientific review panels required to disclose whether they have any financial or other ties to industries or other special interest groups that have an economic or other interest in the outcome of the subject under review?"

A1c: As noted in A1b, the candidates for Panels are required to submit the Confidential Financial Disclosure Report (SF-450). Legal counsel has advised us that this is the only requirement that we can legally make. The Board has embraced the practice of voluntary public disclosure as a means for permitting the sharing of additional information.

Q1d: "Under what circumstances are individuals appointed to serve on special review panels if they could be considered to have such a conflict of interest?"

A1d: As noted above, under 18 U.S.C. Section 208(b)(3) agencies are authorized to waive the restriction where "the need for the individual's services outweighs the potential for a conflict of interest [COI] created by the financial interest involved." Waivers are often granted in matters of recommendations for directions of future research.

Q1e: Have Science Advisory Board Members ever recused themselves from participation in a specific review due to a real or perceived conflict of interest?

A1e: Yes. In the case of dioxin, one Member chose not to participate due to an affiliation with one of the principal protagonists in the matter. A second Member

chose not to participate due to earlier public statements made on the matter.

Q2: "Please provide copies of any written materials relating to the review of potential conflicts of interest of any individuals appointed to, or considered for appointment to, the ad hoc Dioxin Reassessment Review Committee, including any disclosure statements provided by such individuals."

A2: Each member of the Panel submitted a Confidential Financial Information form (SF-450) (Attachment 3). The SAB Staff reviewed these submissions for possible legal conflicts of interest, conferring with the Office of General Council, as needed. As noted above, the SF-450 documents are confidential, and the Agency cannot be released to the public.

The disclosure statements of each of the Panel participants at the May, 1995 meeting were presented orally and are a part of the transcript of that meeting. (See pp. 1-25 of Attachment 7: Transcript of the May 15-16, 1995 meeting the Science Advisory Board's Panel on Dioxin Reassessment Review.)

Q3a: "How does the Science Advisory Board ensure that its review is truly independent of the EPA office that prepared the matter under review?"

A3a: In short, we do the best we can in the face of competing, but equally worthy, considerations. There can be no assurance of absolute independence or absence of bias, but we do take steps to minimize its presence and impact as follows:

Our first consideration is the technical qualifications of the candidates. Because of their technical expertise, many of these individuals will be known to the Agency and may, in fact, have interacted with the Agency on the issue before. This is particularly true for an issue like dioxin that has been attracted the Agency's and the nation's attention for more than two decades. We do make certain that none of the individuals has been directly involved in the production of the Agency's document under review, although, on occasion, we may include--and even seek out--individuals who have participated in earlier peer reviews of the document. The intention is to have a link to any earlier perspectives generated by other independent bodies.

Our second consideration is the possibility of a legal conflict of interest, as discussed above.

Our third consideration is the formation of a balanced panel who collectively have the breadth of knowledge and experience to address all of the issues under discussion and who collectively represent a range of scientific points of view on the issues. Experience on the SAB and elsewhere has indicated that providing a balanced panel is an effective way to minimize the impact of subtle biases and predispositions.

We also provide an opportunity for the voluntary, public sharing of information about the Panelists' backgrounds so that other Panelists and the public can evaluate for themselves how much those respective backgrounds might color the views expressed.

Q3b: "Are appointments to specific scientific review committees made solely within the SAB? What role or influence, if any, do EPA personnel outside of the SAB have in such appointments?"

A3b: As noted above, the actual appointment of Members to the SAB are made by the Deputy Administrator, through a process that is informed by input from the SAB Staff Director.

In the case of Panelists appointments, also described above, the SAB Staff Director makes the decisions based on recommendations from the SAB Staff and the Panel Chair, informed by--but not determined by--input from the Agency.

Q3c: "Did EPA personnel outside of the Science Advisory Board have any role or influence in making appointments to the ad hoc Dioxin Reassessment Review Committee?"

A3c: The procedures followed in the case of the Dioxin Panel were consistent with the process described above. If anything, the SAB was more circumspect than usual about the participation of the Agency in selecting the Panel members, given the amount of the public interest in the issue.

It was the judgment of the Executive Committee--the parent committee of the Dioxin Reassessment Review Panel--that the Panel should be structured around the existing Indoor Air Quality/Total Human Exposure Committee and the Environmental Health Committee. The SAB Staff and the SAB Chair determined who would chair the enterprise.

In short, the Dioxin Reassessment Review Panel was a creature of the Board, by the Board, and for the Board.

A more detailed discussion of the Dioxin Panel Selection process is contained in "Panel Selection for SAB Review of EPA's Dioxin Reassessment", February, 1996. [Attachment 8]

Finally, for your information, I am enclosing a copy of my reply to Admiral Zumwalt, who raised some of these same issues in a letter to the Administrator last month [Attachment 9].

If you have any questions about these answers, in particular, or more generally, about any other aspects of the SAB, please do not hesitate to contact me at TELE--260-4126; FAX--260-9232; or INTERNET--barnes.don@epamail.epa.gov.

Sincerely,

Donald G. Barnes PhD
Staff Director
Science Advisory Board

Attachment 1: "Science Advisory Board" (a brochure)
Attachment 2: SAB FY94 Annual Staff Report: The Year of Reinvention, October, 1994
Attachment 3: "Selection of Consultants for Science Advisory Board Panels", Drafted Jan., 1995
Attachment 4: "SAB Membership Search/Selection Process", February 16, 1996
Attachment 5: Confidential Financial Information form (SF-450)
Attachment 6: "Policy for Public disclosure at SAB Meetings" and attached "Mock Disclosure", August 4, 1996 revision.
Attachment 7: Pages 1-25 of the transcript of the May 15-16, 1995 meeting the Science Advisory Board's Panel on Dioxin Reassessment.
Attachment 8: "Panel Selection for SAB Review of EPA's Dioxin Reassessment", February, 1996
Attachment 9: Barnes to Zumwalt reply to issues raised in the latter's January 2, 1996 letter to the Administrator, February 22, 1996.

Work is coordinated by an Executive Committee led by the Chair of the SAB working with the Chairs of each Standing Committee and additional SAB members. Committees may also enlist the expertise of consultants.

Work of the Board and its committees is facilitated by the SAB Staff Office, which assists in identifying issues; outlining particular projects; arranging for public meetings; and writing, producing, and distributing reports. The staff and its Director are EPA employees.

SAB Committee meetings are conducted in public sessions announced in the Federal Register two to four weeks in advance. Each meeting provides an opportunity for public participation.

What are some examples of the SAB's work?

Many SAB reports focus on studies of specific chemicals and their effects upon health and the environment and on the Agency's internal scientific needs.

The Board reviews all EPA risk assessment guidelines, particularly innovative risk assessments. Much attention was focused on its reviews of new Agency exposure and assessment approaches for "dioxins." The Board has also reviewed alternatives for disinfecting public drinking water supplies and offered a number of reviews on the Environmental Monitoring and Assessment Program, a major research initiative.

At the request of Congress, the SAB has reviewed the President's annual budget requests for the EPA Office of Research and Development.

In 1988 the Board released a major report, *Future Risk*, which recommended an environmental research strategy. At the request of the Administrator the SAB established a new committee to provide advice on the Agency's science research, planning process, direction, and results. In 1990, the Board widely distributed a report, *Reducing Risk*, enunciating the need to set environmental protection priorities on the basis of risk and to develop strategies to deal with emerging environmental problems.

The Board also published a self-examination, *The Mission and Functioning Report*, which sets forth the views of the members on the SAB's history and future.

To keep its members and interested citizens up-to-date, the SAB Staff Office publishes a monthly newsletter, *HAPPENINGS*, informing readers about recent development, upcoming activities, and insights in to operation of the Board.

For further information

SAB information and reports are available from:

SAB Staff Office (A-101)
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460
Telephone (202) 260-4126 260-6552
FAX (202) 260-9232

SAB
Science Advisory Board

What is the Science Advisory Board?

The Science Advisory Board (SAB) of the U.S. Environmental Protection Agency is a body of independent experts who provide advice to the EPA Administrator on scientific and engineering issues.

Why does it exist?

Scientific investigation is more likely to reveal reliable technical information if its design, execution, and results are examined broadly and objectively. Such "sound science" can be furthered by examination and validation through review by outside, independent experts.

Who are members of the SAB?

The SAB's 80 members and more than 300 consultants include scientists, engineers, and other specialists drawn from a broad range of disciplines — physics, chemistry, biology, mathematics, engineering, ecology, economics, medicine, and other fields. The men and women of the SAB come from a variety of organizations doing scientific work — academia, industry, and independent laboratories. Members are appointed by the Administrator to two-year terms.

The variety of backgrounds in this diverse and technically well-qualified group helps to ensure a balanced range of outside views on the Board. Such balance, in fact, is required by the Federal Advisory Committee Act (FACA) — the law under which the Board operates.

Members are compensated by EPA for their time and expenses while doing SAB work, but no member may be a full-time employee of the Federal Government.

What does the SAB do?

Congress established the SAB and gave it a broad mandate to advise the Agency on technical matters. For the most part, the SAB's agenda is set by specific requests from EPA and by recommendations of the members themselves. Some of the Board's activities are specified in various environmental laws. For example, the Clean Air Act and the Safe Drinking Water Act direct that the SAB review technical support documents upon which EPA regulatory actions will be based. On occasion, Congress asks for a special review by the Board.

The Board's principal mission includes ...

- Reviewing the quality and relevance of the information being used or proposed as the basis for Agency regulations

- Reviewing research programs and the technical basis of applied programs

- Reviewing generic approaches to regulatory science, including guidelines governing the use of scientific information in regulatory decisions, and critiquing such analytic methods as mathematical modelling

- Advising the Agency on broad strategic matters in science and technology

- Advising the Agency on emergency and other short-notice programs

The Board may also ...

- Conduct special studies at the request of the Administrator to examine comprehensive issues such as environmental research in the future or studies of comparative risk analysis

- Prepare special reports and reviews at the request of Congress

The SAB does <u>not</u> ...

- Recommend regulatory policy or make regulatory decisions

- Conduct original "bench-type" research work. (Such research generally is done by the Agency's own scientists.)

How does the Board operate?

The Board conducts 50 to 60 committee meetings and submits 30 to 40 reports to the EPA Administrator each year. Members serve on one or more standing committees:

- Clean Air Act Compliance Analysis Council
- Clean Air Scientific Advisory Committee
- Drinking Water Committee
- Ecological Processes & Effects Committee
- Environmental Economics Advisory Committee
- Environmental Engineering Committee
- Environmental Health Committee
- Indoor Air Quality/Total Human Exposure Committee
- Radiation Advisory Committee
- Research Strategies Advisory Committee

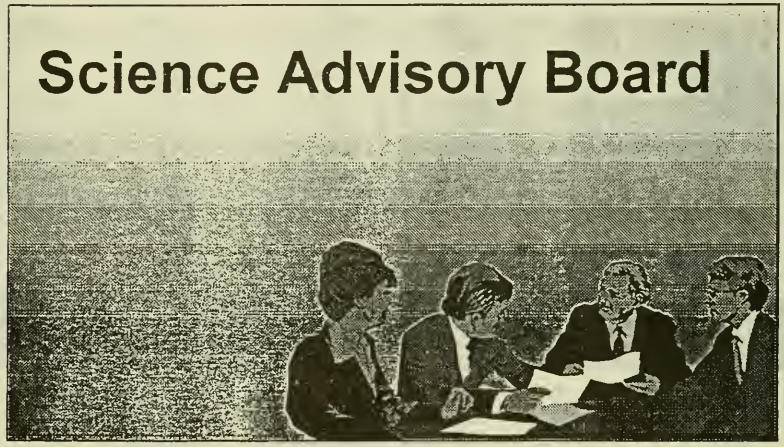
United States
Environmental
Protection Agency

Science Advisory Board
1400
Washington, DC

EPA-SAB–95-001
OCTOBER 1994

EPA SCIENCE ADVISORY BOARD FYI994 ANNUAL STAFF REPORT

The Year of Reinvention



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APPENDIX B1
GUIDELINES FOR SERVICE ON THE SCIENCE ADVISORY BOARD

Background

The Science Advisory Board (SAB) was established in 1974 by the Administrator. In 1978 the SAB received a Congressional mandate to serve as an independent source of scientific and engineering advice to the EPA Administrator.

The SAB consists of approximately 100 Members, who are appointed by the Administrator. These members serve on specific standing committees. The Chairs of the Committees also serve as members of the Executive Committee, which oversees all of the activities of the Board.

In many of its activities, the members of the Board are supplemented by Consultants, who are appointed by the SAB Staff Director after conferring with the Chair of the Committee on which the consultant is to serve. Also, on occasion, Panels will be supplemented by "liaison members" from other governmental agencies. These people are invited by the Staff Director to participate in an ad hoc manner in order to bring their particular expertise to bear on a matter before the Board.

Both the Executive Committee and the permanent Committees may choose to conduct issue-specific business through Subcommittees that are chaired by SAB members. Reports from Subcommittees are reviewed by the respective permanent Committees. The Executive Committee reviews all reports, independent of their origin, prior to formal transmission to the Administrator. The sole exceptions are reports from the Clean Air Scientific Advisory Committee and the Clean Air Act Compliance Analysis Council, which are a separately chartered FACA committees operating within the SAB structure.

Criteria for Selection of Members and Consultants

The SAB is chartered as a Federal Advisory Committee, subject to the rules and regulations of the Federal Advisory Committee Act (FACA) (Public Law 92-463). The charter provides guidance and restrictions on selection of SAB members. The four most significant of which are:

a) Members must be qualified by education, training and experience to evaluate scientific and technical information on matters referred to the Board.

b) The composition of Board committees, subcommittees and panels must be "balanced", representing a range of legitimate technical opinion on the matter.

c) No member of the Board may be a full-time government employee.

d) Members are subject to conflict-of-interest regulations.

The scientific and technical quality and the credibility of those selected is a paramount consideration. Secondary factors considered include the geographic, ethnic, gender, and academic/private sector balance of committees. Other factors that contribute to, but do not determine, the selection include demonstrated ability to work well in a committee process, write well, and complete assignments punctually.

Nominations for membership/consultantship on the Board are accepted at any time. On a biannual basis, the SAB Staff Office publishes a notice in the Federal Register formally soliciting the names of candidates for SAB activities.

Terms of Appointment

Members serve at the pleasure and by appointment of the Administrator. In order to provide suitable terms of service and to insure the infusion of new talent, the following guidelines are generally followed:

Members are generally appointed in October for two-year terms which may be renewed for two additional consecutive terms. Chairs of the standing committees are also appointed for two-year terms which may be renewed for one additional term. If a member is appointed as Chair, this term of service (2-4 years) is added to whatever term of service he/she may accrue as a member. For example,

Years as member	Followed by years as Chair	Followed by years as member	Total years
2	0	0	2
2	2 or 4	0 or 2	4-6
4	2 or 4	0	6-8
6	2 or 4	0	8-10

Reappointment as a member is possible after a two-year hiatus from the SAB, during which time the individual may be called upon to serve as a consultant for a specific issue.

Consultants are appointed to provide the necessary expertise for specific issues. Their terms of appointment are for one year, beginning at any time, and are renewable annually. Their formal appointments may be continued beyond completion of a given project so that their expertise can be quickly assessed in future with a minimum of paperwork.

In general, interagency liaisons participate for the term of issue resolution only.

Member and Consultant Selection Process

Members are appointed by the Administrator based on nominations forwarded by the SAB Staff Director and the Chair of the Executive Committee. These nominations, in turn, are based on recommendations made by the Designated Federal Official (DFO--the member of the SAB Staff with principal responsibility for servicing standing Committees) and the Chairs of the standing Committees. The DFO has the responsibility for developing a list of candidates, utilizing all credible sources, including members of the SAB, other DFOs, EPA staff, staff at the National Academy of Sciences\National Research Council, trade groups, environmental groups, professional organizations, scientific societies, regulated industries, and the informed public.

On occasion, an *ad hoc* Membership Subcommittee of the Executive Committee has been established to assist in the selection process. This group is consulted about possible names and used as a "sounding board" when decisions are being made about appointments. The Membership Subcommittee's principal role is to maintain the integrity of the process and to probe the extent to which objective selection criteria and procedures are being followed. They also raise questions about adherence to the

Statement of Intent on Women and Minorities, adopted by the Executive Committee in 1990, which was designed to increase the representation of these groups on the Board.

Consultants are appointed by the Staff Director following a similar procedure.

Panel Selection Process

In general, once the Board and the Agency have agreed upon a topic for SAB review, the subject is assigned to one of the standing Committees. The Committee Chair and the DFO have primary responsibility for forming a review Panel (the full Committee or a Subcommittee, as the case may be.) The Panel will contain some or all members of the Committee. In many instances, consultants may also be added to the Panel in order to obtain specialized expertise on the particular issue under discussion.

A key aspect in the Panel selection process is the "charge", the mutually agreed upon description of what the Agency would like the review to accomplish and/or what the SAB expects to focus upon. The most helpful charge is one that prescribes specific areas/questions that need attention and/or answers. At a minimum, the elements of the charge should be sufficiently precise that the SAB can determine what additional consultant expertise is needed to conduct the most helpful review.

Often the DFO begins by soliciting ideas about potential members from the Agency staff who are intimately acquainted with the issue and will therefore are often aware of the most informed people. A conscious effort is made to avoid selecting individuals who have had a substantive hand in the development of the document to be reviewed. At the same time, experience has shown the utility of having some representation from individuals/groups who may have been involved in prior reviews of the issue or the document. The goal is to minimize the appearance or practice of an individual's reviewing his/her own work, while at the same time, maintaining an historical link to earlier deliberations surrounding the document/issue. Once the Agency staff has suggested nominees and provided background information on the individuals, their direct role in the panel selection process is complete. Agency staff, the requesting office, and others may be consulted at a later stage for information about nominees received from other sources.

The goal is to gather a balanced group of experts who can provide an independent assessment of the technical matters before the Board. Discrete inquiries

about the nominees are made with a number of different sources. This might include, for example, making inquiries with editors of newsletters, professional colleagues, and experts who are on "the other side" of the issue. As time and resources permit and controversy demands, names of nominees will be investigated via computer search of their publications and pronouncements in public meetings.

Frequently, a determining factor for selection is the availability of the individual to participate in the public review. In the case of multiple-meeting reviews, the SAB may enlist the assistance of a particularly skilled consultant who cannot attend all meetings, but who is willing to do additional homework and/or participate via conference call.

In some cases, the Panel Chair consults with key members of the Panel for their advice before completing the empaneling process. The final selections for consultants are compiled by the DFO in conjunction with the Chair of the Panel and are submitted to the SAB Staff Director for discussion and appointment.

Conflict-of-Interest and Public Disclosure

The intent of FACA is to construct a panel of knowledgeable individuals who are free of conflicts-of-interest. In this regard, each Panel member must complete a confidential financial information form that is reviewed by the Deputy Ethics Officer to determine whether there are any obvious conflicts-of-interest.

Legal conflict-of-interests generally arise in connection with "particular party matters." In general, the SAB (in contrast with the FIFRA Scientific Advisory Panel (SAP)) does not get involved in "particular party matters," hence, legal conflicts-of-interest are rare on the SAB. However, technical conflicts-of-interest can arise, particularly for participants from academic institutions, in connection with Panel recommendations for additional research studies. In most such cases, the DFO's work with the Panel members to apply for waivers from the conflict-of-interest concerns on this matter. The requests for waivers are evaluated on a case-by-case basis by EPA's Office of the General Council. (The Agency generally determines that the benefits to the country derived from these experts' recommendations for additional research, outweigh any technical conflict-of-interest that might be involved.)

However, the Board is also concerned about "apparent conflicts-of-interest." Consequently, Members and Consultants to the Panel are generally selected from the

ATTACHMENT
Guidelines for Public Disclosure at Sab Meetings

Background

Conflict-of-interest (COI) statutes and regulations are aimed at preventing individuals from (knowingly or unknowingly) bringing inappropriate influence to bear on Agency decisions which might affect the financial interests of those individuals. The SAB contributes to the decision-making process of the Agency by evaluating the technical underpinnings upon which rules and regulations are built. SAB Members and consultants (M/Cs) carry our their duties as Special Government Employees (SGE's) and are subject to the COI regulations.

Therefore, in order to protect the integrity of the advisory process itself and the reputations of those involved, procedures have been established to prevent actual COI and minimize the possibility of perceived COI. These procedures include the following:

a) Having M/C's file, at the time of appointment, Special Form 450, Confidential Statement of Employment and Financial Interest. This form is a legal requirement and is maintained by the Agency as a confidential document.

b) Providing M/C's with written material; e.g., "Ethics in a Nutshell" and a copy of Ethics Advisory 92-11.

c. Delivering briefings to M/C's on COI issues on a regular basis.

The following is a description of an additional voluntary[1] procedure that is designed to allow both fellow M/Cs and the observing public to learn more about the backgrounds that M/C's bring to a discussion of a particular issue. In this way, all parties will gain a broader understanding of "where people are coming from" and provide additional insights to help observers and participants evaluate comments made during the discussion.

[1] Note: The disclosure procedure is voluntary, and members/consultants are not obligated to reveal information contained in their Form 450 that would overwise remain confidential.

"broad middle" spectrum of opinion on the technical issue under discussion. Experience has shown that achieving balance through equal representation of extreme views reduces the chance of achieving a workable consensus--pro or con--that the Agency needs to more forward.

The "public disclosure" (see Attached) process (a standard part of all SAB Panel meetings) is a mechanism aimed resolving the apparent conflicts-of-interest issues. This procedure involves an oral statement (sometimes Panel members supplement this with a written document) that lays out the individual's connection with the issue under discussion; e.g., his/her area of expertise, length of experience with the issue, sources of research grants, previous appearance in public forms where he/she might have expressed an opinion, etc. This recitation of prior and/or continuing contacts on the issue assists the public, the Agency, and fellow Panel members in assessing the background from which particular individual's comments spring, so that those comments can be evaluated accordingly.

Conclusion

These Guidelines are intended to assist the SAB in adhering to the mandates and spirit of the Federal Advisory Committee Act. By following these Guidelines the Board should be well-positioned to provide technically-sound, independent, balanced advice to the Agency. At the same time, they provide assurance that there will be adequate participation by and renewal with well-qualified experts from the various communities served by the Board.

Prepared: Oct 14, 1991
Revised: Nov 26, 1991
Revised: Oct. 12, 1994

ATTACHMENT

23-557 O - 96 - 10

Procedure

When an agenda item is introduced that has the potential for COI--actual or perceived--the Designated Federal Official (DFO) will ask each M/C on the panel to speak for the record on his/her background, experience, and interests that relate to the issue at hand. The following items are examples of the type of material that is appropriate to mention in such a disclosure:

a) Research conducted on the matter.

b) Previous pronouncements made on the matter.

c) Interests of employer in the matter.

d) A general description of any other financial interests in the matter: e.g., having investments that might be directly affected by the matter.

e) Other links: e.g., research grants from parties--including EPA--that would be affected by the matter.

The DFO will also publicly refer to any waivers from the COI regulations which have been granted for the purposes of the meeting.

The DFO will assure that the minutes of the meeting reflect that fact such disclosures were made and, if possible, the nature of the disclosures. In addition, the minutes should describe any situations in which, in the opinion of the DFO, an actual or perceived COI existed and how the issue was resolved.

APPENDIX B2
TYPES OF AFFILIATION WITH THE SAB

Members are individuals who serve on the SAB and who are appointed by the EPA Administrator, normally for a two year term (renewable in two-year increments up to a total of six years). Members are either can be either SGEs or Representatives (see below), although the preference is that they serve as SGEs. They are compensated for their time unless they elect to serve without compensation (WOC). Their travel and per diem expenses are paid. They are subject to conflict of interest laws and fill out all personnel paperwork. Members can vote on issues, although most SAB business is conducted by consensus.

Consultants are individuals who serve on the SAB and who are appointed by the SAB Staff Director, normally for a one-year terms, renewable on an annual basis until either their expertise is no longer needed or they elect to stop serving. Consultants are either can be either SGEs or Representatives (see below), although the preference is that they serve as SGEs. They are compensated for their time unless they elect to serve without compensation (WOC). Their travel and per diem expenses are paid. They are subject to conflict of interest laws and fill out all personnel paperwork. Consultants cannot vote on issues, although most SAB business is conducted by consensus.

Special Government Employees (SGEs) are individuals who are brought "on-board" using a personnel appointment involving a modest amount of paperwork. They are normally compensated for their time unless they elect to serve without compensation (WOC). Their travel and per diem expenses are paid. They are subject to conflict of interest laws and certain postemployment restrictions.

Representatives are individuals who serve on the SAB, but whose economic interests cannot be fully separated from those of their employer. Representatives are chosen because a) the SAB would gain technical benefit from hearing the technical views of the employee and/or b) the employer would not allow their experts to participate in any other way; cf., in some instances, service as an SGE can limit subsequent activities of that expert in future dealing with the Agency on the matter. They do not fill out any personnel paperwork. They are not compensated for their time; travel and

per diem expenses maybe covered by either their employer or EPA. They are not subject to the financial disclosure or conflict of interest laws.

Federal Experts are Federal (other than EPA) employees who participate in SAB reviews because of their peculiar experience and expertise. They speak for themselves as technical experts. They are not compensated for their time by the SAB; however, travel and per diem expenses may be paid. No paperwork other than a Travel Authorization is prepared, in cases in which EPA does the travel. They are subject to their own Agency's conflict of interest regulations, and they do not file an SF-450 (financial disclosure form) with the SAB. They are asked to participate in the formal conflict of interest disclosure at the beginning of SAB meetings, as appropriate. Federal Experts may contribute to the development of the Committee's report, but they do not vote.

Other Terms:

The Chair is the leader of an SAB Committee or Subcommittee. A Committee Chairs is an SAB member selected by the Administrator, informed by advice from the Staff Director. A Subcommittee Chair is usually an SAB member selected by the Committee Chair. Consultants and Representatives do not usually serve as Chairs.

An Invited Expert is an individual with special expertise who is brought to a meeting at SAB expense, but who is not being brought on board as a Member or Consultant. The individual's involvement with the Committee is limited to presentations and discussion. He/she does not work on the report or vote on matters before the Committee. The Travel Authorization reads Invitational Travel.

An Invited Participant is an individual who has been formally appointed as a Member or Consultant but whose paperwork has not been completed prior to the meeting. The person is reimbursed for travel expenses, but cannot receive salary prior to completion of the personnel action (SF-50). A completed SF-450 (financial disclosure form) is needed prior to formal participation on a Panel. The Travel Authorization reads Invitational Travel. He/she may contribute to the report and, in the case of someone invited to serve as a Member, may vote, if the occasion should arise.

APPENDIX B3
SAB MEMBERS FOR FY94

LAST NAME	FIRST NAME	COMM	AFFILIATION	CITY, STATE
Abriola	Linda	EEC	University of Michigan	Ann Arbor, MI
Ayres	Stephen M.	CASAC	Medical College of Virginia, VCU	Richmond, VA
Bailey	Paul	IAQC	Stoneybrook Laboratories Inc.	Princeton NJ
Bair	William	RAC	Battelle Pacific Northwest Labs	Richland, WA
Bean	Judy	DWC	University of Miami, Dept of Epidemiology	Miami, FL
Bockstael	Nancy E.	EEAC	University of Maryland	College Park, MD
Brown	Stephen L.	RAC	Risks of Radiation Chemical Compounds	Oakland, CA
Buffler	Patricia	CASAC	University of California	Berkley, CA
Bull	Richard	DWC	Washington State University	Pullman, WA
Bunn	William	EHC	Mobil Corporation	Princeton, NJ
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Fan-Cheuk	Anna	DWC	California Environmental Protection Agency	Berkley, CA
Ford	Jean	CASAC	Harlem Hospital	New York NY
Freeman	A. Myrick	EEAC	Bowdoin College	Brunswick, ME
Gallo	Michael	EHC	Robert Wood Johnson Medical School	Piscataway, NJ
Gerba	Charles P.	DWC	University of Arizona	Tucson, AZ
Gonzalez-Mendez	Ricardo	RAC	University of Puerto Rico, School of Medicine	San Juan, PR
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Kneese	Allan	EEAC	Resources for the Future	Washington, DC
Kolstad	Charles	EEAC	University of Illinois	Urbana, IL
Kripke	Margaret	EC	M.D. Anderson Cancer Center, U of Texas	Houston, TX
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Liu	Benjamin	CASAC	University of Minnesota	Minneapolis, MN
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Mercer	James W.	EEC	GeoTrans, Incorporated	Sterling, VA
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Perera	Frederica	EHC/EC	Columbia University	New York, NY
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LAST NAME	FIRST NAME	COMM	AFFILIATION	CITY, STATE
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APPENDIX B4
SAB CONSULTANTS FOR FY94

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Alm	Alvin L.	RSAC	Science Applications International, Inc.	McLean, VA
Auerbach	Stanley	EPEC	Oak Ridge National Laboratories	Oak Ridge, TN
Bartell	Steven	EPEC	Oak Ridge National Laboratory	Oak Ridge,TN
Bates	David	RAC	Univ of British Columbia	Vancouver, BC
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Dorn	Philip B.	EPEC	Shell Development Company	Houston, TX
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Feero	William	RAC	Electric Research and Management, Inc.	State College, PA
Fenters	James	CASAC	ITT Research Institute	Chicago, IL
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LAST NAME	FIRST NAME	COMMITEE	AFFILIATION	CITY, STATE
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February 22, 1996 F:\memb\panel.sel
Received from Bob Flaak, drafted in Jan., 1995

SELECTION OF CONSULTANTS FOR SCIENCE ADVISORY BOARD PANELS
Draft SOPs for SAB Staff

Background

Under the provisions of the Federal Advisory Committee Act (FACA), all Federal advisory committees, including the Science Advisory Board, are required to have balanced membership. Balance, in this context, refers to the breadth of technical viewpoints represented during the consideration of scientific, engineering and economic issues. The SAB is committed by both principal and law to convening panels that meet this requirement. In addition, to the extent practicable, the Board will broaden the concept of balance to include appropriate geographical and organizational representation.

The Charter of the Board states that the Board "...will consist of a body of independent scientists and engineers of sufficient size and diversity to provide a range of expertise required to assess the scientific and technical aspects of environmental issues." The Charter goes on to state that the Board is "...authorized to consitute such specialized committees and ad hoc investigative panels and subcommittees as the Administrator and the Board find necessary to carry out its responsibilities."

The Science Advisory Board consists of approximately 100 members who are appointed by the EPA Administrator, and who serve on the ten standing committees and various ad hoc panels of the Board. The bulk of the reviews conducted by the Board are carried out by these standing committee. When additional expertise or balance is needed, these members are supplemented by consultants who are appointed by the SAB Staff Director. In certain cases, an ad hoc panel is created to review a specific issue.

Although every effort will be made to ensure that all SAB panels are balanced, clearly, issues that are more controversial, contentious or complicated will require a more concentrated effort by staff to ensure that the appropriate balance is achieved. During this process, consistency is maintained with the July 1994 EPA Peer Review Policy. The procedure outlined below identifies the primary steps in the process whereby the Board creates balanced panels and how the SAB Staff, and ultimately, the SAB Staff Director makes decisions concerning the selection of consultants.

Types of Review Panels

The Board conducts it operations using several types of review groups. These include the following:

a) Standing Committee - these are one of the ten committees that conduct the bulk of the scientific and technical reviews performed by the Board. These committees consist of between seven and fourteen members who are appointed by the EPA Administrator. Sometimes the committees are supplemented by consultants to the Board. The Committees report to the SAB Executive Committee.

b) Subcommittee - a group formed under one of the ten standing committees, chaired by a member of the Board (usually from that standing committee) and containing a number of members of that parent committee, other SAB members and consultants to the Board. Subcommittees report to its parent committee.

c) ad hoc Panel - a group formed by the Executive Committee, chaired by a member of the Board (usually from the Executive Committee) and containing a number of SAB members and consultants to the Board. Ad hoc panels report to the Executive Committee.

The term "Panel" will be used in this procedural document to include all of the above groups.

Types of Committee Review Operations

The Board conducts consultations, provides advisories and performs reviews. In addition, the Board may also offer unsolicited commentaries on issues of interest. These are defined elsewhere. For the purpose of this procedural document, the term "review" will be used to include all such operations.

Development of the Charge

In general, once the Board and the Agency have agreed upon a topic for SAB review, the subject is assigned to one of the standing committees or an Executive Committee ad hoc panel. The committee Chair and the Designated Federal Official (DFO) have primary responsibility for forming a balanced review panel. A key aspect in the panel selection process is the charge, the mutually agreed upon description of what the Agency would like the review to accomplish and/or what the SAB expects to focus upon. A well-characterized charge is essential to the panel selection process, for it identifies the critical expertise necessary for the review process.

Panel Selection Procedures

a) General - A conscious effort is made to avoid selecting individuals who have had a substantive hand in the development of the document to be reviewed. At the same time, however, experience has shown the utility of having some representation from individuals or groups who may have been involved in prior reviews of the same issue or document. The goal is to minimize the appearance or practice of an individual's reviewing his/her own work, while at the same time, maintaining an historical link to earlier deliberations surrounding the document or issue.

b) Specific Procedures - These are the usual steps taken by the DFO in the panel selection process.

1) Identify the critical issues and areas of expertise needed for the review. This information comes from the written charge, from conversations with EPA Program staff providing the review materials, and from a review of the documents that are the subject of the proposed review.

2) Identify the knowledgeable stakeholders. These include Agency program offices, Laboratories, Regional Offices and other Agency components, other Federal, state or local government organizations, environmental groups, industry or trade organizations, citizen groups or other interested parties.

3) Solicit candidates from appropriate stakeholders. By knowing the issues identified in the charge, these groups can provide the SAB with suggestions to improve the balance of the panel being formed. Candidates may also be obtained from the SAB's periodic Federal register notice soliciting candidates for the Board.

4) The DFO will work with the panel Chair to identify critical needs and to determine which areas of expertise and what individuals will constitute a balanced panel. At this point, the DFO should involve the SAB Membership Subcommittee, soliciting their views on expertise or suggestions on candidates.

5) The DFO will usually develop a simple matrix to identify the expertise needed and the candidates considered. An example of each is given in the lower portion of the matrix:

Charge Element	Expertise Needed	Candidate	Source of Candidate	Address of Candidate
Identifies the specific element of the Charge	identifies the needed discipline or specialty	name of individuals being considered	who provided the name of the candidate(s)	what organization is the candidate from (e.g., industry, etc)
Review of the Adequacy of the Human Health Chapter Carbon Monoxide Air Quality Criteria Document	Toxicology Epidemiology	Dr. R. Smith Dr. S. Jones Dr. L. Brown Dr. D. Moran Dr. J. Jackson	EPA/ORD Panel Chair FR Notice Gen. Motors Gen. Motors and Panel Chair	U. Pittsburgh U. Chicago NRDC Consultant Oak Ridge NL

6) Once primary candidates are identified, the DFO will consult with the Staff Director to identify any remaining issues and to finalize the panel selections. The Staff Director will approve the list of panelists to be recruited and/or to serve on the panel.

7) The DFO will then contact prospective panelists to determine availability and interest, preparing the final roster of panelists.

8) Once this has been completed, personnel paperwork will be initiated for any new consultants. A letter will be prepared inviting each panelist to serve on the panel for the stated purpose. This letter will be signed by the Staff Director.

9) The DFO will prepare a brief summary for the permanent administrative record, including the matrix outlined in 5) above, to identify how balance was achieved for this particular panel.

February 16, 1996 F:\memb\membproc.doc

SAB MEMBERSHIP SEARCH/SELECTION PROCESS

The Members (Ms) of the Science Advisory Board (SAB) are appointed by the Administrator. The Executive Committee of the SAB has adopted guidelines on service on the Board [Ref: Annual Report of the SAB Staff, Appendix B1, "Guidelines for Service on the Science Advisory Board", EPA-SAB-EC-95-001] that have generally been followed by the Administrator, as well.

Historically, the Administrator has made appointments from a list of candidates supplied by the Staff Director following an extensive search process, which is the subject of this document.

The SAB Staff maintains "an open application" policy regarding nominations for membership on the Board. That is, names of potential candidates are accepted from any source at any time.

The SAB Staff Director develops the list of candidates by drawing upon a) input from the SAB Staff, b) input from the public, c) input from the Board, and d) input from the Agency.

Note that the Panel of experts convened to examine a particular issue is usually composed of Members of the SAB and of Consultants to the SAB. Members are appointed by the Administrator to serve on any of 10 standing committees that will review a range of issues. Consultants are appointed by the Staff Director--upon the advice of the SAB Staff, generally with the concurrence of the Chair of the Panel--to participate most often in the review of a single issue.

Additional details on different kinds of affiliations with the SAB can be found in the Annual Report [Ref: Annual Report of the SAB Staff, Appendix B2, "Types of Affiliation with the SAB", EPA-SAB-EC-95-001].

Input from the Staff

The SAB Staff are responsible for tracking the membership rosters of their Committees and for planning changes in membership that are consistent with FACA, the guidelines, and the needs of the Committees to have relevant expertise available to address adequately the issues coming before the Committee.

In carrying out this responsibility, the SAB Staff draw upon their professional knowledge and contacts.

In some instances, the Staff have generalized the task by maintaining a graphical presentation of Committee membership, expertise, and terms of service, projected out over a 5-10 year period. (See attached.) The chart shows when a person with a certain expertise completes his/her term of service, thus necessitating a replacement. This assessment of needs focuses the membership search process. The intent is to apply this long-range planning strategy more uniformly across the Committees.

The selection of SAB Consultants is separate from, but related to, the selection of SAB Members. The SAB Staff play a key role in identifying candidates to serve as Consultants to

participate in reviews of specific issues. The Staff comb a variety of sources in the public and private sectors to gather names of Consultant candidates. For particularly controversial issues, the list of candidates can approach or exceed 100 individuals.

Consultants often develop into good candidates for membership, since participation as a Consultant allows the individual and the Board to mutually assess the level of interest, availability, and effectiveness of the relationship.

Input from the Public

On a generally biannual basis the SAB Staff Director solicits the names of candidates for any and all of the SAB committees via a public notice in the Federal Register. The notice describes the Board, its structure and function, the necessary qualifications for members, and the process for submitting nominations. This solicitation usually results in the submission of the names of about 100 candidates.

On occasion, the Staff will contact specific groups to call to their attention that nominations for SAB membership are being accepted. Such groups have included the American Industrial Health Council (AIHC), the Association of Hispanic Colleges and Universities (AHCU), the Environmental Defense Fund (EDF), and Women in Engineering and Science (WISE). Other groups who have expressed an interest in supplying nominations include the National Association of State Universities and Land-Grant Colleges (NASULGC).

There are plans to extend the solicitation for nominees through the SAB Home Page on the Internet, through news releases to newsletters and professional society publications, and through networking with other professional and advisory groups.

Input from the Board

Each year the SAB Staff work with the Committee Chairs to review the upcoming openings on the Board, to identify needed expertise for each of the Committees, and to suggest the names of candidates to submit to the Administrator. In many cases this process involves some or all of the Members of a given Committee.

Some time ago the Executive Committee established a Membership Search Subcommittee, whose responsibilities have included taking a global view of the list of candidates likely to be submitted to the Administrator, checking for diversity in terms of gender, "address", minority status, and geography. In addition, the Subcommittee serves as a source of counsel to the Staff Director on issues related to membership.

The Staff Director also keeps the SAB Chair informed of developments throughout the candidate selection process.

Input from the Agency

The Agency is also an important, initial source of names of candidates for SAB membership. In many instances the Program Offices have been working a particular technical issue for many

months or even years. Therefore, they have are generally aware of most of the specialists in that field.

The SAB Staff is aware that such suggestions may reflect an inadvertent bias towards individuals who might be favorably disposed toward the Office's project. Therefore, these recommendations are examined with particular care, with an emphasis of assuring balance on the Committee.

There are plans to formalize this process through a solicitation letter from the Deputy Administrator to the Agency asking for the names of candidates to serve on the Board. (A similar procedure is currently followed for obtaining Agency requests for projects that should be placed on the SAB's agenda.) The process would begin in the early spring and be designed to dove-tail with the public solicitation.

The Final Selection

As noted above, the appointment of SAB Members is within the purview of the Administrator, who generally delegates the actual selection to the Deputy Administrator.

The Federal Advisory Committee Act (FACA) lays down the following general criteria for membership:

a. Technically qualified individuals
b. Non-Federal employees
c. A "balanced" Board, which has been interpreted as meaning a range of legitimate scientific points of view. Experience has shown that the Board functions most effectively when its Members are selected from the "broad middle" of the spectrum of technical points of view, rather that from the "wings".

Historically, the selection process has involved the SAB Staff Director's presenting the Deputy Administrator with at least two names for every open slot on the Board's roster. In most cases, the Staff Director has recommended one of the two names and has included a justification for the recommendation.

In some instances, the Deputy Administrator has accepted the recommendations directly. In other cases, he/she has discussed the list with the Staff Director. On one occasion the Deputy Administrator conferred with scientifically oriented AAs before making the final selection, without the Staff Director being present. This year, the Staff Director was asked to confer with the AAs and to include their reaction to the list in his submission.

Within the past decade, the Administrator has not appointed anyone to the SAB whose name has not passed through some version of the process described above.

Procedure

At the beginning of an SAB meeting on a single issue or when an agenda item is introduced that has the potential for COI or other impartiality concerns, the DFO will ask each M/C on the panel to speak for the record on his/her background, experience, and interests that relate to the issues at hand.

The following are examples of the type of material that is appropriate to mention in such a disclosure (please refer to **Attachment A - Mock Disclosure** which provides an example of how an individual can provide their disclosure at an SAB meeting):

a) Research conducted on the matter by the individual or their employer.

b) Previous public pronouncements (particularly those cases in which a specific position is taken), e.g., judicial proceedings such as serving as an expert witness or providing testimony, preparation of articles for general or scientific readership, media appearances (TV, radio, newspapers, etc.), etc.

c) Interests of employer in the matter, and the specific role of the individual in that interest..

d) A general description of any other financial interests in the matter: e.g., having investments that might be directly affected by the matter. Note: Members/Consultants are not obligated to reveal information contained in their SF-450 that would otherwise remain confidential.

e) Other links: e.g., research grants to the individual or their employer from parties--including EPA--that would be related to the matter.

During this disclosure, the M/Cs should not refer to any of their activities as a "conflict of interest". If a real conflict did exist, the DFO would have made that judgment prior to the meeting.

The DFO will also publicly refer to any individual waivers from the COI regulations which have been granted by EPA for the purposes of the meeting. The DFO will assure that the minutes of the meeting reflect the fact that such disclosures were made, and if possible, the nature of the disclosures. In addition, the minutes should describe any situations in which, in the opinion of the DFO, an actual or perceived COI existed and how the issue was addressed.

Executive Branch Personnel

CONFIDENTIAL FINANCIAL

DISCLOSURE REPORT

Instructions for Completing SF 450

A. Who Must File

Your agency will inform you if the position in which you serve or will serve has been designated as requiring confidential financial disclosure. Agencies are required to designate positions at or below GS-15, 0-6, or comparable pay rates, in which the nature of duties may involve a potential conflict of interest. Examples of such duties include contracting, procurement, administration of grants and licenses, regulating or auditing of non-Federal entities, or activities having a substantial economic effect on non-Federal entities. Additionally, all special Government employees (SGE's) (those appointed pursuant to 18 U.S.C. 202(a) to serve no more than 130 days in a period of 365 days) must file, unless exempted or subject to the public reporting system. Agencies may, in limited circumstances, also require certain employees in positions above GS-15, 0-6, or a comparable pay rate to file.

B. Reporting Periods

New entrant reports: The reporting period is the preceding twelve months from the date of filing.

Annual reports: The reporting period is the preceding twelve months ending September 30 (or any portion thereof not covered by a new entrant report). However, no report is required if you performed the duties of your position for less than 61 days during that twelve-month period.

C. When to File

New entrant reports: Reports are due within 30 days of assuming a position designated by your agency for filing (including reappointment as a special Government employee (SGE)), unless your agency requests the report earlier. No report is required if you left another (different) filing position within 30 days prior to assuming the new position.

Annual reports: Reports are due not later than October 31, unless extended by your agency.

D. Where to File

With ethics officials at the agency in which you serve or will serve, in accordance with their procedures.

E. General Instructions

1. Confidential filers must provide sufficient information about their outside interests and activities, as well as those of their spouse and dependent children, so that an informed judgment can be made by agency ethics officials as to compliance with applicable conflict of interest laws and standards of conduct regulations. Therefore, it is important that you carefully complete the attached form. This report is a safeguard for you as well as the Government. It provides a mechanism for determining actual or potential conflicts between your public responsibilities and your private interests and activities, and allows you and your agency to fashion appropriate protections against such conflicts.

2. This form consists of five parts, which require identification of certain specific financial interests and activities. No disclosure of amounts or values is required. You must complete each part (except as indicated for Part V) and sign the report. If you have no information to report in any part or do not meet the threshold values for reporting, check the "None" box. If you are a new entrant or special Government employee (SGE), you are not required to complete Part V; in all other instances, a report is incomplete if any part is left blank.

3. The information to be disclosed on this form is required by regulation. You may include other information beyond these requirements that you wish to disclose for clarification. However, disclosure of any information does not authorize holdings, income, liabilities, affiliations, positions, gifts or reimbursements which are otherwise prohibited by law, Executive order, or regulation.

4. You can combine on one form the information applicable to yourself, your spouse, and dependent children which is required by Parts I, II, and V. (Parts III and IV require disclosures about yourself only.) You may, if you desire, distinguish any entry for a family member by preceding the entry with S if it is for a spouse or DC if it pertains to a dependent child. Joint assets may be indicated by J. Information about your spouse is not required in the case of marriage dissolution, permanent separation, or temporary separation with the intention of terminating the marriage or permanently separating.

5. In the case of references to trades or businesses which do not have publicly traded securities, you must provide sufficient information about these private entities to give the reviewers an adequate basis for conflicts analysis. Thus, you must disclose the location and primary trade or business of private entities, as well as their separate financial interests and liabilities which are not solely incidental to the business. For instance, if your family swimming pool services corporation purchases an apartment house for investment in addition to its pool services business, you will have to disclose the apartment house investment, in addition to the family corporation.

6. In the case of a mutual fund, pension, IRA, or investment account, you must disclose information about portfolio holdings and sources of income, unless the entity is "an excepted investment fund." See definition below. In that case, identify it by name and

indicate "excepted investment fund" in the appropriate block; no further disclosure is required.

7. In the case of a trust, you must disclose information about its underlying assets and sources of income, unless it is an "excepted trust." See definition below. In that case, identify it by name and date of creation, and indicate "excepted trust" in the appropriate block; no further disclosure is required. (Additionally, you may, in rare cases, have an interest in a trust specifically certified by the Office of Government Ethics to be a qualified blind or diversified trust, pursuant to statute; for such qualified trusts, you will also be exempt from disclosures about underlying holdings.)

8. *If you need assistance in completing this form, contact the ethics officials of the agency in which you serve or will serve.*

F. Definition of Terms

o Dependent Child

The term "dependent child" means your son, daughter, stepson, or stepdaughter if such person is either.

(1) unmarried, under age 21, and living in your household; or
(2) a "dependent" of yours within the meaning of section 152 of the Internal Revenue Code of 1986, 26 U.S.C. 152.

o Excepted Investment Fund (EIF)

An "excepted investment fund" is a mutual fund, common trust fund of a bank, pension or deferred compensation plan, or any other investment fund, which is:

(1) widely held;
(2) either publicly traded (or available) **or** widely diversified; and
(3) you neither exercise control over nor have the ability to exercise control over the financial interests held by the fund.

A fund is widely diversified when it holds no more than 5% of the value of its portfolio in the securities of any one issuer (other than the U.S. Government) and no more than 20% in any particular economic or geographic sector.

o Excepted Trust (ET)

An "excepted trust" is one which:

(1) Was not created by you, your spouse, or dependent children; and
(2) the holdings or sources of income of which you, your spouse, and dependent children have no past or present knowledge.

o Honoraria

The term "honoraria" means payments (direct or indirect) of money or anything of value to you or your spouse for an appearance, speech or article, excluding necessary travel expenses. Also included are payments to charities in lieu of honoraria.

o Personal Savings Account

The term "personal savings account" includes a certificate of deposit, a money market account, a savings account, an interest-bearing checking account, or any other form of deposit in a bank, savings and loan association, credit union or similar financial institution. Additionally, any money market mutual fund holding is treated as the equivalent of a personal savings account.

Privacy Act Statement

Title I of the Ethics in Government Act of 1978 (5 U.S.C. App), Executive Order 12674, and 5 CFR Part 2634, Subpart I, of the Office of Government Ethics regulations require the reporting of this information. The primary use of the information on this form is for review by Government officials of your agency, to determine compliance with applicable Federal conflict of interest laws and regulations. Additional disclosures of the information on this report may be made: (1) to a Federal, State, or local law enforcement agency if the disclosing agency becomes aware of a violation or potential violation of law or regulation; (2) to a court or party in a court or Federal administrative proceeding if the Government is a party or in order to comply with a subpoena; (3) to a source when necessary to obtain information relevant to a conflict of interest investigation or decision; (4) to the National Archives and Records Administration or the General Services Administration in records management inspections; (5) to the Office of Management and Budget during legislative coordination on private relief legislation; and (6) in response to a request for discovery or for the appearance of a witness in a judicial or administrative proceeding, if the information is relevant to the subject matter. This confidential report will not be disclosed to any requesting person unless authorized by law.

Falsification of information or failure to file or report information required to be reported may subject you to disciplinary action by your employing agency or other appropriate authority. Knowing and willful falsification of information required to be reported may also subject you to criminal prosecution.

Public Burden Information

This collection of information is estimated to take an average of one and a half hours per response, including time for reviewing the instructions, gathering the data needed, and completing the form. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Associate Director for Administration, U.S. Office of Government Ethics, Suite 500, 1201 New York Avenue NW., Washington, DC 20005-3917; and to the Office of Management and Budget, Paperwork Reduction Project (3209-), Washington, DC 20503. Do not send your completed financial disclosure report to these addresses; it should be filed as indicated above in section D.

SF 450
5 CFR Part 2634 1 (9/92)
U S Office of Government Ethics

Form Approved
OMB No 3209

Executive Branch CONFIDENTIAL FINANCIAL DISCLOSURE REPORT

PARTS I - II

Employee's Name *(Last, first, middle initial)*	Position/Title	Grade	Date of Appointment	Page No

Agency	Branch/Unit and Address	Work Phone	Check box if special Government employee (SGE)
			☐

I certify that the statements I have made on this form and all attached statements are true, complete, and correct to the best of my knowledge	Signature of Employee	Date	Reporting Status ☐ New entrant ☐ Annual

Date Received by Agency	*On the basis of information contained in this report I conclude that the filer is in compliance with applicable laws and regulations (except as noted in "comments" box below)*	Signature of Supervisor/Other Intermediate Reviewer	Printed Name/Title	Date

Signature of Agency's Final Reviewing Official and Title	Date	Comments of Reviewing Officials (Check box if continued on reverse) ☐

(Use additional copies of this form as continuation pages, if necessary to complete any part)

Part I: Assets and Income

None ☐

Identify for you, your spouse, and dependent children 1) each asset held for investment or the production of income which had a fair market value exceeding $1,000 ($5,000 for personal savings accounts) at the close of the reporting period; and 2) each asset or source of income (other than U.S. Government salary or retirement, including the Thrift Savings Plan) which generated over $200 in income during the reporting period ($1,000 for your spouse's earned income, other than honoraria) This includes but is not limited to employers, stocks, bonds, tax shelters, personal savings accounts, realty, mutual funds, pensions, annuities, IRA assets, trust assets, commodity futures, trades and businesses, partnership interests, and honoraria Exclude your personal residence, unless you rent it out, and any earned income of your dependent children If the holding is an excepted trust (ET) or an excepted investment fund (EIF) (see instructions), indicate that in the designated column, and you need not disclose underlying holdings.

Assets and Income Sources (Identify specific employer, business, stock, bond, mutual fund, financial institution, type/location of real estate, etc.)	(X) if no longer held	Nature of Income *(Rent, interest, dividends, capital gains, salary, etc)*	If EIF or ET, so indicate	Date *(Only for honoraria)*
1				
2				
3				
4				
5				
6				
7				
8				

Part II: Liabilities

None ☐

Report liabilities over $10,000 owed to any one creditor at any time during the reporting period (over $10,000 at the end of the period if revolving charge accounts) by you, your spouse, and dependent children Exclude a mortgage on your personal residence unless it is rented out, loans secured by automobiles, household furniture or appliances, and liabilities owed to a spouse, dependent child, or parent, brother, sister or child of you or your spouse

Creditors *(Name and address)*	Type of Liability *(Mortgage, promissory note, etc)*
1	
2	
3	
4	

NSN 7540-01 351-9173

Executive Branch CONFIDENTIAL FINANCIAL DISCLOSURE REPORT

Employee's Name *(Last, first, middle initial)*	Agency	Branch/Unit	Work Phone	Page No

Part III: Outside Positions

None ☐

Report any positions, whether or not compensated, which you held outside the U.S. Government during the reporting period. Positions include but are not limited to those of an employee, officer, director, trustee, general partner, proprietor, representative, or consultant of any corporation, firm, partnership, or other business enterprise or any non-profit organization or educational institution. Exclude positions with religious, social, fraternal, or political entities or those solely of an honorary nature. You need not report any positions of your spouse or dependent children.

Organization *(Name and address)*	Type of Organization	Position	(X) If no longer held
1			
2			
3			
4			
5			

Part IV: Agreements and Arrangements

None ☐

Report your agreements or arrangements for future employment, leaves of absence, continuation of payment by a former employer (including severance payments), or continuing participation in an employee benefit plan. You need not report agreements or arrangements of your spouse or dependent children.

Terms of Any Agreement or Arrangement	Parties	Date
1		
2		
3		
4		

Part V: Gifts and Travel Reimbursements

None ☐

Do not complete this part if you are a new entrant or a special Government employee (SGE).

Report the source and a brief description of gifts from one source totaling $250 or more during the reporting period, and travel reimbursements from one source totaling $250 or more during the reporting period, which are received by you, your spouse, and dependent children. Exclude anything valued at $100 or less, anything from relatives or from the U.S. Government; anything given to your agency in connection with your official travel; and food, lodging, or entertainment received as personal hospitality at the donor's residence or other premises.

Source	Description *(For travel-related items, include itinerary and date)*
1	
2	
3	
4	
5	
6	

POLICY FOR PUBLIC DISCLOSURE AT SAB MEETINGS

Background

The Science Advisory Board (SAB) contributes to the decision-making process of the U.S. Environmental Protection Agency (EPA) by evaluating the technical underpinnings upon which rules and regulations are built. In conducting such evaluations, SAB members and consultants (M/Cs) carry out their duties as Special Government Employees (SGE's), and, as a result, are subject to the COI regulations. Conflict-of-interest (COI) statutes and regulations are aimed at preventing individuals from (knowingly or unknowingly) bringing inappropriate influence to bear on Agency decisions which might affect the financial interests of those individuals, their family members and/or the organizations which employ them.

In order to protect the integrity of the SAB process itself and the reputations of those involved, procedures have been established to address conflict-of-interest and other concerns about members' and consultants' impartiality. These procedures include the following:

a) Having SAB M/Cs file an SF-450, Confidential Financial Disclosure Report (with annual updates, as required);

b) Providing SAB M/Cs with required annual training via written informational material; e.g., "Standards of Ethical Conduct for Employees of the Executive Branch" (5 CFR Part 2635), "Take the High Road," and EPA Ethics Advisories 92-11 and 94-18;

c) Delivering briefings to M/Cs on COI issues on a regular basis.

Through the above procedures and regular, informed contact with M/Cs, the Designated Federal Official (DFO) on the SAB Staff normally identifies actual, as well as perceived, COI issues long before a public meeting occurs. When an actual COI situation is determined to exist, appropriate steps are taken to protect the individual and the process (e.g., either the M/C will recuse him/herself from discussions of the issue, the DFO will seek another M/C to participate in the meeting in lieu of the recused M/C, etc.).

The following is a description of the public disclosure policy, an additional procedure that is designed to allow both fellow SAB M/Cs and the observing public to learn more about the backgrounds that SAB M/Cs bring to a discussion of a particular issue. In this way, all parties will gain a broader understanding of "where people are coming from" and provide additional insights to help observers and participants evaluate comments made during the discussion.

MOCK DISCLOSURE

Or, How to Implement the Policy for Public Disclosure at SAB Meetings

Background

For several years each SAB meeting has had a period of "disclosure", during which panelists orally and voluntarily state their previous involvement with the technical issues before the Board. Each panelist is provided with a copy of "Policy for Public Disclosure at SAB Meetings" as guidance on the type of information to include in the disclosure.

The mock disclosure below is intended to provide further guidance on how the disclosure might proceed. It is assumed, for purposes of this illustration, that the panel is reviewing a risk assessment of buckminsterfullerenes.

Issues and Mock-Responses

a) Research conducted on the matter.

I have conducted research and published results on the thermodynamics and kinetics of the fullerene formation in low temperature flames. In some of this work, I have speculated about the possible occurrence of fullerenes in the environment. This information is relevant to the exposure portion of the risk assessment before us. I have not done any work on the toxicity of fullerenes, although--since I work with these materials routinely--I have both a professional and personal interest in the topic! Consequently, I am aware of a good bit of the literature related to the toxicology of fullerenes.

b) Previous pronouncements made on the matter

In addition to my scientific publications and presentations at professional meetings, I have written one general article for Discover magazine and have appeared in a NOVA TV segment on fullerenes. In the Discover article I did express some caution that in the current somewhat frenetic drive to investigate these unique materials and their physical properties (e.g., superconductivity), it is important that we also investigate the health and environmental risks possibly posed by these substances. I have not appeared in any judicial proceedings related to the risks of these materials.

c) Interests of employer on the matter

My employer--Buckyballs, Inc--is deeply involved in the development and testing of fullerenes for commercial purposes. My responsibilities are limited to the basic science division of the company and have nothing to do directly with product development, marketing, or sales.

After discussing my situation with the SAB Staff and the EPA's Office of General Counsel, it has been determined that I have a legal conflict-of-interest in this review. However, the Agency has determined that my technical contribution is of such importance in this case that the Agency has granted me a waiver which will allow me to participate in this review. The DFO has a copy of the waiver for anyone who would wish to see it.

I want to assure everyone that I will be as professionally objective as I can be on this matter. But I think it is important that you are all aware of the conditions under which my participation is taking place.

d) A general description of any other financial interests in the matter

The SAB Staff have reviewed my Confidential Financial Disclosure statement (Form SF-450) and have determined that, other than my relationship with my employer, I have no other legal conflict-of-interest.

However, I want everyone to be aware that my son is doing PhD work at the University of Cincinnati and has chosen to work in the area of--you guessed it--fullerenes; specifically chlorine derivatives of branched-chain derivatives of C_{60} fullerenes. My principal interest here is in not getting scooped by my own son! He is currently supported by a grant from the National Science Foundation, although his major professor has a grant from the US EPA which supports another graduate student's work on continuous emission monitoring systems (CEMS) for particulate matter in the 10-20 micron range.

e) Other links; e.g., research grants

Early in my career, 20 years ago, I benefitted from an EPA training grant given to the University of Pittsburgh where I took my PhD in synthetic organic chemistry. Before joining Buckyballs, Inc eight years ago, I was an associate professor in the chemistry department at Cornell University. During that period I received grants from a number of governmental sources (not EPA), plus two multi-year grants from the National Alliance for Incineration (NAI), which funded my work in flame chemistry. My first published paper on fullerenes stemmed from work supported by the NAI.

UNITED STATES
ENVIRONMENTAL PROTECTION AGENCY

SCIENCE ADVISORY BOARD

DIOXIN REASSESSMENT REVIEW

Grand Ballroom B-C
Herndon Renaissance Hotel
13869 Park Center Road
Herndon, Virginia 22071

Monday and Tuesday,
May 15 and 16, 1995

9:00 a.m. and 3:45 p.m.

APPEARANCES:

Chair

DR. MORTON LIPPMANN
New York University Medical Center
Institute of Environmental Medicine
Tuxedo, New York

Members

DR. WILLIAM B. BUNN
Mobile Administrative Services Company, Inc.
Princeton, New Jersey

DR. KENNY S. CRUMP
K S Crump Division
Ruston, Louisiana

DR. ERNEST E. McCONNELL
Raleigh, North Carolina

DR. HENRY C. PITOT
McArdle Laboratory for Cancer Research
Madison, Wisconsin

APPEARANCES: (Continued)

Consultants

DR. RICHARD W. CLAPP
B.U. School of Public Health
Boston, Massachusetts

DR. JOHN DOULL
University of Kansas
Kansas City, Kansas

DR. RONALD W. ESTABROOK
The University of Texas
Dallas, Texas

DR. JOHN GRAHAM
Harvard Center for Risk Analysis
Boston, Massachusetts

DR. WILLIAM GREENLEE
Purdue University
West Lafayette, Indiana

DR. NORBERT KAMINSKI
Michigan State University
East Lansing, Michigan

DR. THOMAS MACK
University of Southern California
Los Angeles, California

DR. JOHN McLACHLAN
Tulane University
New Orleans, Louisiana

DR. DAVID OZONOFF
Boston University School of
Public Health
Boston, Massachusetts

DR. GABRIEL PLAA
Department of Pharmacology
Montreal, Quebec, Canada

DR. DONALD REED
Oregon State University
Corvallis, Oregon

APPEARANCES: (Continued)

Consultants

DR. KNUTE RINGEN
Center to Protect Workers' Rights
Washington, D.C.

DR. ALAN SILVERSTONE
SUNY Health Science Center
Syracuse, New York

DR. SIDNEY STOHS, Dean
Creighton University
Omaha, Nebraska

DR. BERNARD WEISS
University of Rochester
Rochester, New York

DR. HANSPETER WITSCHI
University of California
Davis, California

DR. TIMOTHY ZACHAREWSKI
University of Western Ontario
London, Ontario, Canada

Federal Experts

DR. MICHAEL GOUGH
U.S. Congress OTA
Washington, D.C.

DR. MICHAEL I. LUSTER
NIEHS/NIH
Research Triangle Park, North Carolina

DR. THOMAS UMBREIT
CDRH/FDA
Rockville, Maryland

APPEARANCES: (Continued)

Exposure Panel

Chair

DR. JOAN DAISEY
Lawrence Berkeley Laboratory
Berkeley, California

Members

DR. PAUL BAILEY
Mobil
Princeton, New Jersey

DR. ROBERT HAZEN
Bureau of Risk Assessment
State of New Jersey
Trenton, New Jersey

KAI-SHEN LIU
California Department of Health Services
Berkeley, California

THOMAS E. McKONE, Ph.D.
University of California
Davis, California

DR. MARIA MORANDI
University of Texas Health
Science Center at Houston
Houston, Texas

DR. JONATHAN M. SAMET
Johns Hopkins University
Baltimore, Maryland

DR. WILLIAM RANDALL SEEKER
Energy and Environmental Research Corporation
Irvine, California

RON WHITE
American Lung Association
Washington, D.C.

APPEARANCES: (Continued)

Consultants

DR. RONALD HITES
Indiana University
Bloomington, Indiana

DR. NANCY KIM
New York State Department of Health
Albany, New York

DR. DENNIS PAUSTENBACH
McLaren/Hart/ChemRisk
Alameda, California

DR. JOHN JAKE RYAN
Bureau of Chemical Safety
Ottawa, Ontario, Canada

DR. VALERIE THOMAS
Princeton University
Princeton, New Jersey

Designated Federal Officials

SAMUEL RONDBERG
Science Advisory Board (1400F)
U.S. Environmental Protection Agency
Washington, D.C. 20460

A. ROBERT FLAAK
Science Advisory Board (1400F)
U.S. Environmental Protection Agency
Washington, D.C. 20460

Staff Secretary

MARY L. WINSTON
Science Advisory Board (1400F)
U.S. Environmental Protection Agency
Washington, D.C. 20460

A G E N D A

A G E N D A

PROCEEDINGS

9:00 a.m.

Opening Comments

Monday, May 15, 1995

DR. LIPPMANN: Good morning.

We ask everybody to please take their seats. We do need to start on time.

On behalf of the Science Advisory Board Committees arrayed around this table and their consultants, I'd like to welcome everybody in the audience to this meeting, to review the dioxin risk assessment documents prepared by the agency staff and their contractors.

This is an extremely tight schedule, and a very, very large committee. I hope we can all be brief and to the point throughout this exercise; otherwise, we just can't possibly finish our -- our review.

This is a very important document, a very contentious document. You -- most of all of you, certainly everybody on the panel, has seen all the documents, six volumes, plus all the material that was sent to you by the various interested parties.

Clearly, we have our work cut out for us, and I don't want to take any more time in introduction. I'll turn -- I'm Dr. Lippmann from New York University.

I'll be chairing the Health Panel and working with my colleague, Dr. Daisy, who is chairing the Exposure Panel, and we will be responsible for the integration of the two documents at the end.

I'll turn the microphone over to Sam Rondberg, Science Advisory Board DFO, who will be giving us his introductions and some of our marching orders about procedures we have to follow for this public meeting.

Committee Introduction

MR. RONDBERG: Thanks, Mark.

Just for those of you who are not into the archei of the Federal Advisory Committee Act, DFO is designated federal official. By law, every government advisory committee has to have a federal staff person who makes sure that the rules and regulations concerning advisory committees are followed. That's the last I'll talk about that.

I actually serve as executive secretary, is the real description of the function that I provide.

Just a little bit of administrativia before we get to the substance of the day, primarily for members of the committees.

We'll be having lunch in the rooms. The Exposure Panel will withdraw with their cigars and

brandy and so forth to the room next door, and the Health Panel will be dining in here. I'll need to get a count later of how many people from each group are choosing to buy lunch. It's going to cost you about $19, but it's a fairly nice buffet. Sorry about that. The restaurant here is just too small to be able to handle us and turn the group over in the time that we need to get back to work. So, we're dining in.

Very briefly, if you take a look at the folders that were in front of your place at the table, there is a huge raft of paper in there, just in case that you were running short of paper from the stuff that you got in the mail. The usual things, like the agenda and the committee roster is in there.

There is a piece of paper labeled "Procedures for Public Disclosure SAB Meetings", which you need to take a look at, and we'll be going over that in a minute. Robert Flack, who's the assistant staff director of the Science Advisory Board, and is serving as the executive secretary and DFO for the Exposure Panel for this, will be leading the group through that as, hopefully, quickly as possible.

Of a more substantive nature, you will find some additional reading materials in there. A blue book that's produced by the Environ Corporation for the

American Paper Institute, and some plain white paper with some additional materials that have been submitted by the public since the last mailing.

There is a submission from a Dr. Hardell in Sweden, who is taking issue with how some of his data has been used by other public commenters. Dave Bayliss has a submission, and I believe that's just those two are in there.

One last administrativia. If any of you had any administrative problems concerning your travel or something, a bit later, we'll have two of the SAB administrative support staff sitting outside. They can change travel arrangements for you or if you have some other problem with your hotel accommodations, reservations or anything like that. I know some of you may have had to stay somewhere else.

Barring -- and you also find the forms to fill out to get reimbursed for your travel and your other expenses.

With that, let me turn it over -- unless someone has a question on procedure, turn it over to Bob Flaak to lead you through the disclosure part of the meeting.

MR. FLAAK: Thank you, Sam.

One thing I'd like to remind all of the panel

members, the court reporter has a very difficult task today to maintain track of who's speaking, and to keep track of everything that's being put into the transcript.

So, as a reminder, and we'll remind you as we go through the course of the meeting, please be sure to speak at one of these microphones, and if one of them isn't immediately in front of you as you are about to make a comment, I ask that you either drag it over near you or have one of your colleagues near you bring it over closer to you, so the court reporter can pick up everything that you say.

For members of the audience that have a comment to make, and once they get recognized by the Chair, I ask that you use the microphone that's standing up in the middle of the audience, the free-standing mike. Come up, state your name and whatever your comment might be, so again we can get that into the record.

The podium that sits in the middle of the room, once we're through with the presentations and such, will be moved out of the way. So, those of you who are sitting somewhat behind it, we'll see if you're sleeping, and we'll move it out of the way.

Okay. One thing I'd like to do now, I'd like

to start on our public disclosure process. This is something that we do at all of our SAB meetings, and it's a means whereby those of you in the audience and the other members around the table can determine something about the backgrounds of the other members of the panel, and the sorts of activities they might have been involved in with regard to the issue that we are looking at.

Now, this is different than conflict of interest. Conflict of interest is something that we deal with long before this meeting comes to the public view, and that's something that Sam and I have a responsibility for and making sure that individuals who sit at the table are not in a conflict of interest situation, which creates severe problems for them as well as for the agency as we do this kind of a review.

What I'm asking the panel members to do today is to go through a brief discussion of their activities that relate to certain areas, which I'll identify in just a moment.

The way we normally do this is we go around the table and ask each individual to answer these five or six questions. We found in the past with a panel about half this size it takes over an hour. So, we're going to shorten the process a little bit and do it a

little differently this morning, and instead of doing it that way, I'm going to go through the questions one at a time and canvas the panel as a group for each of these questions.

Let me read the questions first, so you can understand what it is I'm talking about. We ask panel members whether they've done any research on this issue before, and I suspect that's probably going to be true for most of you. I'm not looking for a lengthy discourse on this.

Any previous pronouncements you've made. In other words, have you been an expert -- prepared expert testimony. Have you been an expert witness on this issue before this agency or any other agency, in particular? Does your employer have particular interest in this matter? Any financial interests you have in this particular matter? For example, does a panel member own stock in a company that produces the issue that we're discussing? And other individual links you might have, research grants from EPA, for example, on issues related to dioxin.

So, with that in mind, let me go through the questions first, one at a time, and ask the panel members, I'll just go around the room briefly, and ask if any of you have any specific areas where you might

have some disclosure you wish to make on these items, bearing in mind that we have looked at the confidential financial disclosure statements of every member of this panel and identified no such conflicts that exist with regard to the work that we are dealing with today.

This is primarily a sense of where people are coming from. So, let me ask the first question.

On research conducted on this matter, does anybody have anything they wish to raise?

Let me start with Bob Hazen and around that end of the table. Bob, do you have anything in specific?

DR. HAZEN: No, I don't believe there are any issues of concern for me.

MR. FLAAK: All right. Coming down that side of the table, I don't necessarily need a negative from everybody, but coming down, does anyone on this side of the table have any research issues they wish to identify? If so, please raise your hand on this side of the table. On the far side of the table. On this side of the table. Okay.

Has anyone made previous pronouncements on this matter? Have they been expert witnesses or provided testimony? Again, starting on your end, Bob.

DR. HAZEN: No, I haven't.

MR. FLAAK: Okay. Are you speaking for everybody? Anybody on this side of the table?

DR. BAILEY: No, I haven't.

MR. FLAAK: Down this end over here?

DR. McKONE: I think I should point out --

MR. FLAAK: Please identify yourself.

DR. McKONE: Oh. Get the microphone to work.

MR. FLAAK: Is it working? Okay.

DR. McKONE: I was one of the reviewers of the first day's document. Tom McKone.

MR. FLAAK: Anybody else on this side? Yes?

DR. GOUGH: Yes. Do you include being an expert witness at a trial?

MR. FLAAK: Right.

DR. GOUGH: Okay. Michael Gough. I was an expert witness in two trials concerning dioxin exposure in 1989 and '90, perhaps, when I was not a federal employee.

MR. FLAAK: Okay. Anybody on this side? I'm sorry?

DR. CRUMP: This is Kenny Crump. From the period of about 1980 to about 1995, I have testified in probably about a half a dozen trials involving dioxin, one of which is still active.

DR. LUSTER: I testified many years ago for

the EPA on the EPA Dow hearings for dioxin.

DR. OZONOFF: I'm Dave Ozonoff. I've testified in the Times Beech trial which involved dioxin exposures maybe seven-eight years ago. No active cases, though.

DR. PAUSTENBACH: Yes. Dennis Paustenbach. I've been involved in two or three trials in recent times, and probably half a dozen depositions, and I don't have any pronouncements that I've made before the agency before, but I did serve in the last peer review, I think it was '87.

DR. KIM: I'm Nancy Kim. I guess the only thing that's applicable to me is I served on the last peer review panel, too.

MR. FLAAK: Anybody else on that side of the table? Yes?

DR. KAMINSKI: I'm Norv Kaminski, and I served on the National Academy of Sciences committee to review the health effects of herbicides on Vietnam veterans.

MR. FLAAK: Anybody at the front table?

DR. CLAPP: I'm Richard Clapp, and I testified before the congressional committee of, I think it was, Veterans Affairs about health effects of Agent Orange, and I've also testified in two trials having to do with dioxin in St. Louis.

MR. FLAAK: Anybody else at the front table?

(No response)

MR. FLAAK: Our third question deals with your -- oh, I'm sorry, John.

DR. DOULL: I've been involved in a couple of trials, also, now that I recall.

MR. FLAAK: Anybody else?

(No response)

MR. FLAAK: All right. The third question deals with the interests of your employer in the matter.

Does anybody's employer have a particular interest in this issue?

Bob, again, let me start on your side.

DR. HAZEN: Well, yes, I'd say the State of New Jersey has a particular interest in this issue.

MR. FLAAK: Thank you, Bob. Anybody else on this side? Yes, sir?

DR. UMBREIT: My employer has some interest in this, although not the particular center I work for.

MR. FLAAK: Anybody else on this side?

DR. UMBREIT: With the building trades, our members have interests in this.

DR. WHITE: Ron White with the American Lung Association, and our organization has an interest in

this issue, also.

DR. McKONE: Tom McKone. I believe the Lawrence Livermore Laboratory, who I work for, has been trying to build some sort of an incinerator. I've not been involved with that activity, but it is an issue there.

MR. FLAAK: Anybody else on this side?

(No response)

MR. FLAAK: On the other side? Nancy?

DR. KIM: I'm Nancy Kim. I work with New York State. New York State is interested in dioxin issues. I guess since I wasn't really sure what the research aim meant, I guess I should also say that we have been involved in looking at dioxin exposure in the state office building, in several landfills, and some fish and dairy issues, too.

MR. FLAAK: Anybody else on that side of the table?

DR. PAUSTENBACH: Yes, I'm with a consulting firm, and we -- people within the firm certainly do some dioxin consulting. I've tried to avoid it for awhile now.

MR. FLAAK: Okay.

DR. THOMAS: I'd like to go back to this issue of research and just point out that I have done

research on sources of dioxin and made my own admission inventory.

MR. FLAAK: Valerie and any of the others, make sure to identify yourselves, so the court reporter catches who you are. Sometimes it's hard to catch the names.

Anybody else on this side?

DR. RYAN: My name is John Ryan from Canada, and our federal agency is in Canada, and we are involved in the regulation.

MR. FLAAK: Anyone else on this side? Yes?

DR. OZONOFF: I'm Dave Ozonoff. I also work for the Department of Veterans Affairs, and they certainly have an interest in this.

MR. FLAAK: Anyone at the front table?

DR. SILVERSTONE: Al Silverstone. I, like Nancy Kim, am an employee of the State of New York, though in the university system, and our hospital, which is a state university hospital, is trying to get an incinerator approved. I also have research grants on the effects of dioxin on immune system development.

DR. McCONNELL: Gene McConnell. I have designed or helped design and evaluate studies of PCBs, several types of PCBs. These studies are on-going at the present.

DR. BUNN: I'm Bill Bunn. I'm with Mobil Corporation. We have the usual industrial interest in these and other related compounds, not felt to be different than general industry.

MR. FLAAK: Anybody else on the front table?

(No response)

MR. FLAAK: Anybody else on this question?

(No response)

MR. FLAAK: All right. The next question deals with the general description of any financial interest you have in the matter. Much of these are covered. Those of you as you recall having filled out your confidential financial disclosure statements may have included some of these things in there. These are not things we're asking you to disclose. We're just asking for any general financial interest you might have in this matter. Chances are beyond what you had in that disclosure form, there may not be any others.

Are there any financial interests in this particular issue? Anybody?

(No response)

MR. FLAAK: All right. The last question deals with research grants from parties, including EPA, that would be affected by this matter.

Is anyone involved in research grants,

particularly from EPA, that might be affected by this matter?

Take Bob's side again, for the start. Anybody over here?

DR. McKONE: Tom McKone. I receive quite a bit of funding from the State of California, Environmental Protection Agency, to look at multi-media exposure modeling that's quite related to this, and some of that funding is actually -- the state's grants come from the EPA through cooperative agreements. So, it's indirectly EPA-funded.

DR. REED: I'm Donald Reed, Oregon State University, and I'm Director of the Environmental Health Sciences Center at Oregon State. Within that center, we have responsibility for a program grant that is on the toxicity of halo carbons, and members who participate in that research, some of them are doing research on dioxin.

MR. FLAAK: Anybody else on this side?

DR. SAMET: I'm Jon Samet. I have no direct funding from parties involved in this. I am Chair of the Department of Epidemiology at Johns Hopkins, which is -- there is a large industry-funded study of paper workers in progress in my department. I have no direct involvement with that project.

MR. FLAAK: Thanks. The other side? Anybody over here?

DR. SEEKER: Yes. I'm Randy Seeker from EER Corporation. My company has a contract to help support the EPA in the development of their new max standards for hazardous waste incinerators.

DR. HITES: Ron Hites from Indiana University. I have research grants from the National Science Foundation on dioxin and other pending applications to do research on dioxin.

DR. KIM: Nancy Kim. There are several parts of the health department, the laboratories and research may have grants from EPA or other funded -- funding groups, which I am not aware of.

I also know that my part of the agency has applied for a grant with EPA to look at dioxin exposure.

DR. OZONOFF: I'm Dave Ozonoff from Boston University, School of Public Health. I'm chair of the department that has grants from NIEHS, where the money actually comes from EPA, and I'm the Director of the Super Fund Basic Research Center, which has dioxin-related research in it. That center is funded by EPA money, although it is administered by NIEHS.

MR. FLAAK: All right. Thank you. Anybody

else on this side? Yes?

DR. GREENLEE: I'm Bill Greenlee from Purdue University. In addition to funding from NIH, I have received research grants from the American Forest Paper Association and General Electric, and I've also received gifts for research from Chemical Manufacturers Association and Dow Chemical.

MR. FLAAK: Anybody else on this side?

DR. KAMINSKI: Yes. My name is Norv Kaminski from Michigan State University. I have a research grant from the NIEHS to study the immunotoxicity by PCDD.

I think I also should mention, I'm not sure which category this should fall under, but I have and continue to serve as a consultant for Dow-Corning pertaining to interactions between silicone products and the immune system.

MR. FLAAK: Thank you. Anybody else on the head table here? On this end? Anybody down this end yet?

DR. SILVERSTONE: Al Silverstone. I've been -- I'm listed as a consultant on an EPA contract with the Syracuse Research Corporation on toxic chemicals, although I've not been asked to do anything yet.

DR. STOHS: Sid Stohs, Creighton University. We have funding from the Air Force Office of Scientific Research involving various halogenated pesticides, and there's some work that does relate to dioxins.

DR. WEISS: Bernie Weiss from the University of Rochester. We have a grant from the International Life Sciences Institute to pursue questions about the developmental toxicity of PCDD.

MR. FLAAK: Are there anybody -- anyone else on the panel have anything else to say about this?

(No response)

MR. FLAAK: Okay. I think we're ready to start the presentations. I'm going to turn the mike back over to Mort Lippmann, the chair, so we can begin with the process of the meeting.

Thank you.

DR. LIPPMANN: Okay. Well, the chair is also not involved in any of these issues. I have EPA research money but nothing related at all to dioxin.

We'll move on to the first set of public comments. We have public comments for the group as a whole, and we have other time for public comments on the health issues or the exposure issues separately.

I will ask -- oh, I'm sorry. We'll come back to the public comments momentarily.

February 23, 1996 F:\proj\dioxpane.doc

PANEL SELECTION FOR SAB REVIEW OF EPA'S DIOXIN REASSESSMENT
Sam Rondberg's 2/20/96

EPA released the final draft of the Dioxin Reassessment in mid-October, 1994; on December 20, 1994, ORD provided a draft Charge to the SAB Staff.

Pursuant to earlier discussions by the SAB Executive Committee, Dr. Matanoski requested that the SAB Staff work with the Chairs of the IAQC (Dr. Daisey) and EHC (Dr. Perera) to negotiate a final Charge and organize a joint review of the reassessment document. Soon after receipt of the Charge, Dr. Perera decided that (because of her position on the NRDC Board of Directors) it would be inappropriate for her to Chair the EHC for this particular review, and recused herself from the activity. Soon afterward, Dr. Matanoski asked Dr. Morton Lippmann to assume the Health Panel Chair [in place of[Dr. Perera and to lead the overall dioxin review activity.

Once a draft Charge was in hand, the SAB Designated Federal Official for this project (Mr. Samuel Rondberg) began identifying possible candidates, based on recommendations from SAB Staff, the Chairs of the Health and Exposure Panels, ORD Staff, and on recommendations previously volunteered by several industry groups. During the process, SAB staff also queried the Audubon Society, Greenpeace, the National Resources Defense Council, and the Environmental Defense Fund for recommendations. Some of the individuals contacted as potential consultants also provided additional recommendations -- typically co-workers, former students, etc. From the totality of the names assembled, the Chairs and SAB staff selected a "short-list" for the Health and Exposure Panels. Persons on the two lists were then contacted to determine their willingness to serve, and screened for <u>overt</u> conflict situations (such as participation in groups planning to present an advocacy position at the SAB meeting or having already taken a strong public position on the issues to be discussed). Several potential candidates on the short-list were eliminated as a result of this screen.

All persons willing to serve, and who passed the initial conflict "screen" were then provided with a copy of the draft Charge (for either Health or Exposure, as appropriate) and asked to identify (in rank order) the three issues they would prefer to work on if selected for the review. Although the specific discipline of each individual was already identified, it was felt that self-assignment to issue would yield the best possible match. At the same time, the process to enroll as Consultants those persons not already "on-board" as current SAB Members or Consultants was started. Each of these persons completed an SF 450 (Financial Disclosure Statement) as part of this process. Review of the disclosure statements by the DFO and Assistant SAB Staff Director did not disclose any conflict situations, and none

of the selected panelists was disqualified from participating. One Consultant to the Exposure Panel was recused from commenting on the findings of the Health Panel because of prior activities of his employer concerning dioxin health effects.

Once the self-assignments were completed, SAB Staff arrayed the selections against the 23 questions in the Health Charge and 20 questions in the Exposure Charge and discussed the distribution with the Chairs. The resulting consensus was to invite all respondents for the Health Panel (save one, who was dropped to avoid having two individuals from the same university and department on the Health Panel) and for the Exposure Panel to participate, schedules allowing. The driving factor behind this decision was to have in-depth coverage for all 43 issues, as well as to have the Panels constitute a broad and balanced range of backgrounds and outlook.

The individuals "surviving" this selection process were then queried as to availability during the months of April and May, 1995; May 15/16 were then selected as the two days with the greatest number of panelists available. Individuals who had listed those two days as "Not Available" were contacted, and in some cases, persuaded to revise their schedules in order to participate. This process ultimately resulted in 25 Members/Consultants (M/C) for the Health panel and 14 for the Exposure Panel. Once Membership stabilized, the tentative assignments of M/Cs to specific issues was revised and "Leads" assigned for each issue.

Table 1 lists the participants in the two panels, their affiliation, and SAB status.

Table 1-- Affiliation of Panelists

AFFILIATION	HEALTH		EXPOSURE	
	Number	Percent	Number	Percent
ACADEMIC	18	72	5	36
INDUSTRY	1	4	1	7
CONSULTANT	2	8	2	14
FEDERAL GOVT.	3	12	1***	7
STATE GOVT.	0	0	3	22
OTHER	1	4	2	14
TOTAL	25*	100	14*	100**

*Includes Chair
**Actual total less due to rounding
***Canadian Govt.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

February 22, 1996

E.R. Zumwalt, Jr.
Admiral USN (Ret)
Chairman, Agent Orange Coordinating Council
1000 Wilson Blvd. Suite 3105
Arlington, VA 22209-3901

Dear Adm Zumwalt:

I am responding to your January 2, 1996 letter to Administrator Browner requesting her to "administratively make the decision not to use "Corporate Docs" (scientists who receive grants, compensation, consulting fees, etc. from corporations who produce dioxin as a by-product of their manufacturing processes) on the Science Advisory Board."

I want to provide you with some additional information about how your concerns are addressed in rules that govern the operations of advisory committees, such as the Science Advisory Board, and how they are implemented at the SAB.

Regarding conflict of interest in general, under 18 U.S.C. Section 208(a), Federal employees, including "special government employees" that serve on the Science Advisory Board, are barred from participating in any "particular matter" which affects their employers' financial interests. However, under 18 U.S.C. Section 208(b)(3) agencies are authorized to waive the restriction where "the need for the individual's services outweighs the potential for a conflict of interest [COI] created by the financial interest involved."

Regarding these rules and the SAB, the SAB generally doesn't deal with particular matters and, specifically, dioxin is not a particular matter because it is widespread in the environment and because the Agency's reassessment was aimed at dioxin wherever it is found and from whatever sources it might come--from food to incinerators, from volcanoes to pulp and paper, from human milk to chemical companies.

As a part of the process of assessing whether such a legal COI exists or not, each member of an SAB Panel (i.e., Members and Consultants) must submit a financial disclosure report that is reviewed by staff, with legal counsel as needed, prior to the meeting. By law, EPA cannot make this information available to the public.

As a Federal advisory committee, an SAB panel is required to include a balance of points of view on the technical issues it addresses. Achieving such a balance is a challenge, particularly in a case as enduring and controversial as dioxin. One method of seeking balance is to have a large and diverse group of participants, so that no one point of view dominates the proceedings. In the case of the dioxin review, we enlisted 39 different scientists who were qualified to examine dioxin issues and who came from a wide spectrum of institutions and backgrounds from across the country. Some of these scientists may have received research support from corporations associated with dioxin-containing materials. We recognize that some observers may believe that this fact would affect the participants' views on the technical issues considered by the panel; however, we believe that the importance of hearing their technical input outweighs this concern.

The SAB has also adopted a practice of voluntary "public disclosure" at the beginning of its meetings on specific issues. During the disclosure exercise, the panelists may share with their colleagues and members of the public information about their backgrounds that might be relevant to the issue at hand; this may include sources of funding.

As you and I discussed at the Greenpeace offices late last year, the SAB is continually seeking to make improvements in our process, including the issue of perceived conflict of interest. An SAB subcommittee will present recommendations for such improvements at the public Executive Committee meeting on the afternoon of Feb. 28 to be held in the Administrator's Conference Room (Rm 1103, West Tower, Waterside Mall, 401 M St. SW, Washington, DC). The intent is to have a process that is open, fair, and informed.

In closing, I want to state that I do not agree with your general characterization of any scientist who might receive a grant from a particular industry as a "pseudo scientist" or a "Corporate Doc". Such a broad, prejudicial characterization is both unwarranted and unsubstantiated. The history of the SAB is replete with examples of men and women of science who have served the country well with the highest level of credibility, and professionalism, regardless of their professional backgrounds and current employment. Our system, however imperfect, is designed to solicit the views of a wide range of credible voices on technical issues, so that a consensus position can emerge in full view of the public.

I would be happy to discuss these matters further with you and explore suggestions for improving the process within the limits of the law. Thank you for your continuing interest in the Science Advisory Board.

Sincerely,

Donald G. Barnes, PhD
Staff Director
Science Advisory Board

cc. Administrator Carol Browner
Deputy Administrator Fred Hansen
SAB Executive Committee

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