REGULATION OF TOBACCO PRODUCTS
(Part 2)

HEARINGS

BEFORE THE

SUBCOMMITTEE ON
HEALTH AND THE ENVIRONMENT

OF THE

COMMITTEE ON
ENERGY AND COMMERCE
HOUSE OF REPRESENTATIVES

ONE HUNDRED THIRD CONGRESS

SECOND SESSION

APRIL 28, MAY 17 AND 26, 1994

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REGULATION OF TOBACCO PRODUCTS

THURSDAY, APRIL 28, 1994

HOUSE OF REPRESENTATIVES,
COMMITTEE ON ENERGY AND COMMERCE,
SUBCOMMITTEE ON HEALTH AND THE ENVIRONMENT,
Washington DC.

The subcommittee met, pursuant to notice, at 10 a.m., room 2123 Rayburn House Office Building, Hon. Henry A. Waxman (chairman) presiding.

Mr. WAXMAN. The meeting of the subcommittee will come to order. This hearing is a continuation of the subcommittee's oversight hearings on tobacco products. The witnesses this morning are Dr. Victor DeNoble and Dr. Paul Mele.

Dr. DeNoble worked in Philip Morris's behavioral pharmacology laboratory from 1980 to 1984. During most of that time, he directed animal research on nicotine and substances that might be substituted for nicotine. Dr. Mele worked with Dr. DeNoble in his laboratory.

On March 31, I released a study that Dr. DeNoble had coauthored with Dr. Mele and that demonstrated that nicotine has reinforcing properties, which the National Institute of Drug Abuse has stated is a hallmark for addiction. The study was accepted for publication in 1983, and again in 1986, but each time, Philip Morris directed Dr. DeNoble to withdraw it. As a consequence, it was never published.

Today, Dr. DeNoble and Dr. Mele are here to testify about these incidents and others during their employment at Philip Morris. To my knowledge, they are the first scientists to be released from their confidentiality agreements by a tobacco company.

On behalf of the subcommittee, I want to welcome Dr. DeNoble and Dr. Mele, and to say that we are pleased that they are willing to testify in the subcommittee's oversight hearings on tobacco products. But before calling on the two of you, I want to recognize members for any opening statements they wish to make, and to recognize Mr. Bliley first.

Mr. BLILEY. Thank you, Mr. Chairman. Today we will hear in greater detail about an issue that was raised at the subcommittee's last two tobacco hearings, research on nicotine undertaken by former Philip Morris research scientists in the early 1980's.

And, as with the other tobacco-related issues that this subcommittee has recently considered, this issue already has been aired in the press. It is therefore critically important that, once again, our deliberations attempt to separate fact from fiction, and that we opt for good policy rather than good headlines. I hope that

we approach the proceedings today from the benefit of a wisdom that can only be achieved through experience.

In this case, the experience is very recent because we have been down this road before. Just a month ago, allegations were flying in the media about nicotine spiking. In response, top executives from the major tobacco companies came before us voluntarily and under oath to put these unfounded claims to rest and to set the record straight. Hopefully, the process will allow for a similar fair hearing for all concerned regarding this issue.

In conclusion, I am here to listen. But because we have the benefit of hearing only one side of the issue here today, additional questions surely will arise. Therefore, this hearing should be viewed as but part of a larger process that allows both sides of the issue to be properly aired.

Mr. WAXMAN. Thank you, Mr. Bliley. I agree with your comments that this is one part of a series that will be available for us to get the information to the subcommittee.

Mr. Synar?

Mr. SYNAR. Thank you, Mr. Chairman. As early as 40 years ago, researchers informed Americans of the harmful effects of smoking. The industry continues to deny the deadliness of smoking. On April 14th of this year, the CEO's of the seven major U.S. tobacco companies flatly denied, while under oath, that nicotine is addictive and that smoking causes cancer.

Today, Dr. Victor DeNoble, the former associate senior scientist with Philip Morris, will tell us a different story. His testimony will directly contradict the tobacco executives' statements that nicotine is not addictive, and it will show that the companies have proof of nicotine's addictiveness.

Now, why do our executives continue to deny it? Because to do anything else would subject them to expensive and immediate liability. This concealment, coupled with the industry's continued direct targeting of children, is criminal.

Americans are beginning to demand some answers from tobacco companies, not to bring back the 8 million lives lost, but to prevent the next generation of children from taking up this addiction that will, in all likelihood, result in their deaths.

I look forward to this important and revealing accumulation of information today in the continuing battle with the largest preventable cause of death in our society.

[The opening statement of Mr. Synar follows:]

STATEMENT OF HON. MIKE SYNAR

As early as 40 years ago, researchers informed Americans of the harmful effects of smoking. In the years since the 1964 Surgeon General's Report on Smoking, the tobacco industry has continuously denied the deadliness of smoking.

On April 14, 1994, the CEO's of the seven major U.S. tobacco companies flatly denied, while under oath, that nicotine is addictive and that smoking causes cancer. Today, Dr. Victor DeNoble, former Associate Senior Scientist with Philip Morris, will testify concerning an article entitled, "Nicotine as a Positive Reinforcer in Rats: Effects of Infusion Dose and Fixed Ratio Size", which he submitted to *Pyschopharmacology* on May 16, 1983. His article, never published because he was forced to retract it by Philip Morris, concluded that "all the rats initiated and maintained nicotine self-administration." This directly contradicts the tobacco executives' statements that nicotine is not addictive. It shows the companies had proof of nicotine's addictiveness.

This concealment, coupled with the industry's direct targeting of children, is criminal. American Tobacco Company, which sold off its tobacco products line this week, saw the writing on the wall. Americans are beginning to demand some answers from tobacco companies—not to bring back the 8 million lives lost—but to prevent the next generation of children from taking up the addiction that will, in all likelihood, result in their deaths.

Mr. WAXMAN. Thank you very much, Mr. Synar. Mr. Wyden?

Mr. WYDEN. Thank you very much, Mr. Chairman. I too want to commend you for the painstaking approach you are taking on the health hazards of tobacco. I think of this series of hearings as an effort to get at the core of the onion by peeling away the deceptive practices we have seen in this industry layer by layer. Today's hearing is especially important because we have a respected researcher, a former tobacco industry scientist who, in effect, is brought in from the cold.

Now, this is no spy novel. But the whole environment of the tobacco industry and its relationship to tobacco consumers very often does read like a cloak-and-dagger thriller. This industry works with secret lists, confidential technologies, and veiled advertising messages. And, in effect, through these practices, can orchestrate a world-class confidence game.

Individuals like Dr. DeNoble who get in their way because of embarrassing information they might have to offer are, in effect, pushed to the sidelines. And it seems to me the losers are consumers who each day by the tens of thousands decide to take up this deadly habit.

Now, the corporate leaders who run this industry have told the subcommittee, in sworn testimony, that they have no proof that their products are addictive. Recently they came before us and said that they are making a safe product that millions of Americans enjoy. In effect, their message was that the United States Congress was the bad guy for trying to dampen enthusiasm for a harmless vice.

But the fact of the matter is that all Americans ought to be troubled by what we are going to learn today, which is that when the tobacco industry does research and the results hurt them, the investigators and their data are buttoned up tight. What we are learning is that tobacco science is politicized science. And it is especially important that we have Dr. DeNoble's message today.

Mr. Chairman, I look forward to pursuing this with you. You have taken, in my view, another important step by bringing Dr. DeNoble here, and I look forward to our questions.

Mr. WAXMAN. Thank you very much, Mr. Wyden.

Dr. DeNoble and Dr. Mele, we are pleased to welcome you both to our subcommittee hearing today. You were both employed as research scientists by Philip Morris during the early 1980's. I understand, Dr. DeNoble, that you are going to make a statement, but that Dr. Mele wishes simply to be available to answer questions.

But before we get to your testimony, I want to inform you that the applicable rules of the House and the rules of the committee are in that blue and white pamphlet that is on the table before you. They will inform you of the limits on the power of this subcommittee and the extent of your rights during your appearance today.

Do you desire to be represented by counsel, or advised by counsel, during your appearances today?

Mr. DENOBLE. Mr. Chairman, I do have counsel with me, and I would like the opportunity to talk with him, if necessary.

Mr. WAXMAN. OK. Dr. Mele?

Mr. MELE. Yes. I would likewise.

Mr. WAXMAN. Do you object to appearing before the subcommittee under oath?

Mr. DENOBLE. No, sir, I do not.

Mr. MELE. No.

Mr. WAXMAN. OK. If you have no objections to appearing before us under oath, I'd like to ask you both to rise and raise your right hand.

[Witnesses sworn.]

Mr. WAXMAN. Please consider yourself to be under oath. I'd like to ask each of you to identify yourself for the record.

Mr. DENOBLE. I'm Dr. Victor John DeNoble.

Mr. MELE. I am Dr. Paul C. Mele.

Mr. WAXMAN. And would you introduce anyone who is with you today? Could you be sure the mike is turned on? There is a button that pushes forward.

Mr. DENOBLE. I have with me my wife, Chum DeNoble, and my counsel, Eric Snyder.

Mr. MELE. Yes. I have my wife, Joy Mele; my son, Tristan Mele; my counsel, Dave Vladeck.

Mr. WAXMAN. Thank you. Dr. DeNoble, I'd like to recognize you to make your comments.

Mr. DENOBLE. Thank you.

Mr. WAXMAN. Would you pull the microphone close to you so that we can be sure to get all of this on the record?

TESTIMONY OF VICTOR JOHN DENOBLE, SENIOR BEHAVIOR ANALYST, DELAWARE COMMUNITY MENTAL RETARDATION PROGRAM, ACCOMPANIED BY PAUL C. MELE, ARMED FORCES RADIOBIOLOGY RESEARCH INSTITUTE

Mr. DENOBLE. Mr. Chairman and members of the committee, I am Dr. Victor John DeNoble, and this is my colleague and friend, Dr. Paul Mele. We are grateful to have this opportunity to talk to you about our research.

Mr. WAXMAN. Excuse me, Dr. DeNoble. I'm not sure your mike is on. Is your light on?

Mr. DENOBLE. The light is on, yes, sir.

Mr. WAXMAN. Pull it closer to you then.

Mr. DENOBLE. My career began in 1976 when I received a Ph.D. in experimental psychology from Adelphi University in New York. After receiving my degree, I began post-doctoral research on the behavioral and the electrophysiological effects of alcohol in non-human primates at Downstate Medical Center, in New York.

Following this, I accepted a post-doctoral position sponsored by the National Institute of Drug Abuse at the University of Minnesota. At Minnesota I studied the self-administration techniques in rodent, non-human primates. I am currently a senior behavioral analyst with the Community Mental Retardation Program for the State of Delaware.

From April of 1980 to April of 1984, I was employed at the Philip Morris Research Center in Richmond, Va., as an associate scientist;

and then as an associate senior scientist, a position I was promoted to in 1983. During that time, I established and directed a behavioral pharmacology laboratory to study the behavioral and physiological effects of nicotine in rats.

Our goal was to identify the effects of nicotine in the central nervous system, and to establish structure activity relationships among organically synthesized analogues of nicotine. The purpose of this nicotine analogue program was to develop an analogue that would retain the physiological effects of nicotine in the brain as well as the behavioral effects, but not have adverse effects on the cardiovascular system. Our program was successful in identifying a series of compounds which met this criteria.

In order to behaviorally evaluate nicotine analogues, a characterization of the behavioral effects of nicotine in rats using a variety of offered conditioning procedures needed to be developed. One of the earliest test procedures we used was a nicotine self-administration test. In this procedure, an animal can press a lever and deliver a drug solution into its vein. If the solution has reinforcing properties or qualities, the animal will continue to press the lever.

We found that nicotine functioned as an intravenously delivered reinforcer in rats in the absence of any inducement conditions. In previous studies, inducement conditions made the analysis of nicotine's reinforcing effects difficult to assess. Our result demonstrated for the first time that nicotine shared common characteristics with other drugs that are delivered intravenously.

In other studies, we also found that rats would develop tolerance to repeated injections of nicotine, and this tolerance was in part behavioral and in part physiological. Following tolerance development, higher doses of nicotine were required to produce the effects that were both quantitatively and qualitatively similar to before tolerance development.

We also examined the potential of nicotine to produce a physical dependence in rats. In two separate experiments, we were not able to show that nicotine produced a withdrawal syndrome.

There were several other studies performed in the laboratory with nicotine. And although none of these—very few of these studies were published, almost all of this research has since been replicated, confirmed by other investigators around the world.

In 1982, however, we began to investigate the behavioral effects of another smoke component. To the best of my knowledge, this research has never been replicated and therefore awaits scientific confirmation. In our search to identify molecules in cigarette smoke that may have reinforcing properties other than nicotine, we identified a molecule called acetaldehyde. It was in high concentrations in cigarette smoke.

Because acetaldehyde could be delivered to the brain in seconds, and is highly reactive with catecholamines, we hypothesized that, one, acetaldehyde functions as a reinforcer for rats; and, two, that possibly interactions with nicotine could be achieved. Our research confirmed that acetaldehyde was a reinforcer for rats, and the reinforcing properties of acetaldehyde and nicotine combinations would interact producing additive effects in these animals.

I would like to state that senior research management in Richmond, Va., as well as top officials of the Philip Morris Company in

New York, continually reviewed our research and approved our research. Senior management also reviewed and made final decisions determining whether data could be published, presented at scientific meetings, or even discussed in the scientific community.

With regard to the Philip Morris press release, dated March 31st, 1994, the statements made concerning my research and my assessment of the self-administration experiments are out of context and misleading. Further, during my employment with Philip Morris, three manuscripts were approved for publication. Two of these manuscripts were subsequently ordered to be withdrawn by the company after this approval.

In addition, a 1983 scheduled presentation of the nicotine self-administration paper at the American Psychological Association meeting was also blocked by the company. Finally, without prior discussion or prior warning, the behavioral pharmacology laboratory was abruptly closed in April of 1984.

Mr. Chairman, and members of the committee, I would like to thank you for reading our statement, and I welcome any questions.

[The prepared statement of Dr. DeNoble follows:]

STATEMENT OF VICTOR JOHN DENOBLE

Mr. Chairman and members of the committee, I am Dr. Victor John DeNoble, a behavioral psychologist, and I am senior behavior analyst for the Community Mental Retardation Program for the State of Delaware. I am grateful to have this opportunity to discuss my research at this hearing on tobacco.

From 1980 to 1984, I was employed at the Philip Morris Research Center in Richmond, Virginia as an associate senior scientist. My responsibilities were to establish and direct a behavioral pharmacology laboratory to study the behavioral and physiological effects of nicotine and other smoke components in rats. Our initial goal was to identify the behavioral effects of nicotine on the central nervous system and to establish structure activity relationships among organically synthesized nicotine analogues. The purpose of the nicotine analogue program was to develop an analogue that would retain physiological and behavioral effects in the brain and be devoid of any pharmacological effects in other organs, specifically, the cardiovascular system. In order to accomplish this goal, a characterization of the behavioral effects of nicotine in rats using a variety of operant conditioning procedures needed to be developed.

With regard to the nicotine analogue program, our primary behavioral test was a nicotine drug discrimination procedure. Rats were trained to identify whether they had been injected with nicotine or saline. Using nicotinic-cholinergic antagonists, we demonstrated that the rats ability to discriminate (identify) whether it was injected with nicotine or saline was mediated by nicotine's effect in the brain not by nicotine's effect on the peripheral nicotinic receptors.

This test procedure was used to identify nicotine analogues that would mimic the effects of nicotine in this discrimination procedure. This behavioral data was then combined with nicotinic receptor binding data, as well as peripheral pharmacology data generated outside Philip Morris Research Center to develop structure-activity relationships among these analogues. The goal of this program was to identity a nicotine analogue that would have central nervous system effects without effects on the cardiovascular system.

In our self-administration studies we demonstrated that: (1) nicotine functioned as an intravenously delivered reinforcer for rats; (2) that rats would press levers several times for a single injection; (3) that nicotine self-administration was controlled, at least in part, by nicotine levels in blood or tissue; (4) that the reinforcing effects were mediated by central nicotinic-cholinergic receptors; (5) that endogenous opioid receptors did not mediate nicotine's reinforcing effects and, finally; (6) that termination of chronic self-administration of nicotine over several weeks did not result in observable behavioral signs of a physiological dependence.

With regard to this last observation, we extended our findings by examining the effects of nicotine self-administration on concurrent lever pressing maintained by food. Concurrent nicotine self-administration was shown not to interfere with lever pressing for food and that discontinuing access to nicotine self-administration did

not alter the rate or pattern of food intake. In a related experiment, we examined the effects of pharmacological antagonism of chronic nicotine administration on lever pressing maintained by food. The results showed that antagonism of chronically administered nicotine also did not result in a disruption of schedule-controlled behavior.

Termination or antagonism of chronic nicotine administration did not result in a disruption of lever pressing for food suggesting that chronic administration of nicotine did not result in a physiological dependence in these tests.

Studies on the development and loss of tolerance to chronic nicotine exposure revealed that tolerance to the behavioral effects of nicotine developed following chronic administration of nicotine. The study design allowed us to demonstrate that both physiological and behavioral tolerance develops to chronic nicotine administration. Following tolerance development, higher doses of nicotine were required to produce effects that were both quantitatively and qualitatively similar to those observed before tolerance had developed.

Our laboratory also conducted a series of studies on the behavioral effects of nicotine when injected directly into the ventricles of the brain, as well as, when nicotine is injected into different brain sites. This research was directed at identifying the neuroanatomical substrates mediating the behavioral effects of nicotine. These test procedures also became a primary screening tool for the nicotine analogue program since the behavioral effects of nicotine were shown to be controlled by nicotine's effect on the brain, not on peripheral systems.

The above mentioned studies summarizes major research efforts with nicotine and nicotine analogues. There were several other experiments which provided support for these major research programs.

Almost all of the research that occurred between 1980 and 1984 has subsequently been replicated, confirmed and extended by other investigators around the world.

However, in 1982 we began to investigate the behavioral effects of another smoke component. To the best of my knowledge, this research has never been replicated, and therefore, awaits scientific confimation.

In our search to identity other molecules in tobacco smoke that may have reinforcing properties, we identified acetaldehyde as a major component of gas phase smoke. Tobacco itself does not contain acetaldehyde, but, as a product of pyrolysis, large amounts of acetaldehyde are formed and delivered in the gas phase of smoking. Interest in this molecule began in the mid-1960's when it was demonstrated that another aldehyde, formaldehyde, was shown to condense with endogenous catecholamines to form compounds called tetrahydroisoquinolines (TIQ's). In the mid 1970's, it was demonstrated that acetaldehyde, a major metabolite of alcohol could also form TIQ's. TIQ's have been hypothesized to act as "false neurotransmitters" in catecholamine-containing neurons, The fact that acetaldehyde is in high concentration in smoke, is delivered to the brain in seconds, and is highly reactive with catecholamines led us to hypothesize that: (1) acetaldehyde may function as an intravenously delivered reinforcer for rats; (2) that the reinforcing effect would be mediated by the formation of TIQ's; and that, (3) interactions with nicotine's reinforcing effects would be possible.

Our research confirmed that acetaldehyde was: (1) a reinforcer when delivered intravenously; (2) that rats would press levers several times for a single injection; and (3) that termination of acetaldehyde access did not result in observable signs of a physiological dependence. In a related series of experiments, we further demonstrated that the reinforcing properties of nicotine and acetaldehyde would interact behaviorally producing additive effects in rats.

These results formed the basis for the hypothesis that both nicotine and acetaldehyde are reinforcing agents in cigarette smoke and that their interaction would result in an enhanced reinforcing effect in humans.

I would like to thank you for allowing me to place my statement in the record.

Mr. WAXMAN. Thank you very much, Dr. DeNoble. If the members have no objection, we're going to recognize each one in turn for 10 minutes, but since these are our only witnesses for today, if someone is pursuing a line of questioning that might go a little beyond the 10 minutes, I hope we'll be willing to extend the courtesy to continue that line of questioning.

Dr. DeNoble, I want the clerk to give you Exhibit 1, which is your resume. And I note that you've published more than 20 articles, and that you have held teaching positions at 7 universities.

[The document follows:]

CURRICULUM VITAE

VICTOR J. DeNOBLE
1200 Camp Woods Court
Newark, DE 19711

Telephone: Home: (302) 234-1196

EDUCATION:

B.A.	Psychology	Adelphi University, N.Y. 1971
M.S.	Experimental Psychology	Adelphi University, N.Y. 1974
Ph.D.	Physiological Psychology	Adelphi University, N.Y. 1976

Title of Dissertation:

Response Acceleration and Suppression Produced by Response-Independent Food Presentation in Rats with Septal Lesions. Presented at the Eastern Psychological Association, 1974. Published JCPP 91:107-117, 1977. (Advisor: Dr. M. A. Caplan)

National Institute of Drug Abuse Postdoctoral Fellow: University of Minnesota, Department of Pharmacology and Psychiatry, MN 1978-1980 (Sponsors: Dr. Richard A. Meisch, Dr. Roy Pickens and Dr. Travis Thompson)

Current Position:

Senior Behavior Analyst, Department of Mental Retardation, Delaware State Mental Health Department

RESEARCH EXPERIENCE:

1991 - 1992 Manager, Development and Training, R&D Operations, Du Pont Merck Pharmaceutical Company, Experimental Station, Wilmington, Delaware.

1990 - 1991 Research Associate, Central Nervous System Research, The DuPont Merck Pharmaceutical Company, Experimental Station, Wilmington, Delaware.

1987 - 1990 Research Associate, Central Nervous System Research, E. I. DuPont de Nemours & Co., Inc., Experimental Station, Wilmington, Delaware.

1984 - 1987 Research Associate, CNS Research, Ayerst Laboratories Research, Inc., Princeton, New Jersey.

1983 - 1984 Associate Senior Scientist, Project Leader, Behavioral Pharmacology Laboratory, Philip Morris Research Center, Richmond, Virginia.

1980 - 1983 Project Leader, Behavioral Pharmacology Laboratory, Philip Morris Research Center, Richmond, Virginia.

RESEARCH EXPERIENCE (cont'd):

1978 - 1980	Research Associate, Psychiatry Research Unit, University of Minnesota.
1976 - 1977	Research Associate, Department of Biopsychology and Anatomy, Downstate Medical Center, Brooklyn, New York.
1974 - 1977	Senior Research Scientist, Electrophysiology Laboratory, Department of Psychiatry, Downstate Medical, Brooklyn, New York.

TEACHING EXPERIENCE:

1989 - 1990	Adjunct Associate Professor, Department of Psychology, University of Delaware, Newark, Delaware.
1986 - 1987	Adjunct Assistant Professor, Department of Psychology, Trenton State College, Trenton, New Jersey.
1983 - 1986	Adjunct Associate Professor, Department of Psychology, Virginia Commonwealth University, Richmond, Virginia.
1977 - 1978	Adjunct Associate Professor, Department of Psychology, State University of New York, Farmingdale, New York.
1976 - 1978	Adjunct Assistant Professor, Department of Psychology, City University of New York, Brooklyn College, New York.
1973 - 1976	Adjunct Lecturer, Department of Psychology, City University of New York, Brooklyn College, New York.
1975 - 1977	Adjunct Lecturer at State University of New York, Farmingdale.
1972 - 1976	Adjunct Lecturer at Adelphi University.

GUEST REVIEWER FOR:

Neuropsychopharmacology
Science
Pharmacology Biochemistry and Behavior
Physiological Psychology
Physiology and Behavior
Life Sciences
1984 Division 28 - American Psychological Association
1985 Division 28 - American Psychological Association

PUBLICATIONS:

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DeNoble, V. J. Chairperson, DuPont's Animal Welfare Committee, 1987-1989.

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Mr. WAXMAN. Dr. Mele, we are also pleased that you are able to be here. And although you didn't present a formal statement, could you tell us about your training, education, and employment background?

Mr. MELE. Yes. First, Mr. Chairman, let me thank you and the members of the committee for allowing me to be here today. I received my Ph.D. degree in experimental psychology in 1980 from Adelphi University, in the field of behavioral pharmacology. That work focused on the effects of amphetamine on complex behavior in rats.

Following that work, I spent 2 years at the University of Wisconsin at Madison, funded under a National Institute of Health research service award, where I studied the behavioral toxicology of lead and polychlorinated biphenyls in non-human primates.

Following that, I went to the Philip Morris Research Center, to work with Dr. DeNoble. That was in November of 1981, and I was there until its closing in April of 1984.

Since leaving Philip Morris, I have been with the Department of Defense, at the Armed Forces Radiobiology Research Institute, in Bethesda, studying effects of ionizing radiation and radioprotectant compounds on the behavior of laboratory animals.

Mr. WAXMAN. Thank you very much, Dr. Mele.

Dr. DeNoble, I assume that you are aware that a month ago Dr. David Kessler, the Commissioner of the Food and Drug Administration, testified before this subcommittee about nicotine manipulation. He referred to your article on nicotine self-administration in rats and to the fact that Philip Morris ordered the article withdrawn after it had been accepted for publication. Subsequent to his testimony, I released your article.

Then just 2 weeks ago, the executives from the largest tobacco companies appeared before this subcommittee and testified that nicotine is not addictive. For example, William Campbell, the president and CEO of Philip Morris, U.S.A., testified, and I quote, "Cigarette smoking is not addictive. Nicotine contributes to the taste of cigarettes and the pleasure of smoking."

Now, you ran a laboratory that was charged with identifying the essential characteristics of nicotine so that a synthetic form of nicotine could be developed, yet you didn't test for the taste of nicotine. Did you ever hear of any serious discussion to the effect that Philip Morris leaves nicotine in cigarettes for taste?

Mr. DENOBLE. No, sir, none at all.

Mr. WAXMAN. As I understand it, you were charged with developing a rat model to test nicotine analogues for the effects on the brain in an effort to develop a nicotine substitute. Did anyone at Philip Morris ever suggest to you during the course of your analogue work that you should develop an analogue that would duplicate the taste of nicotine?

Mr. DENOBLE. No, not at all.

Mr. WAXMAN. Are you aware of anyone else doing work on this at Philip Morris?

Mr. DENOBLE. Our laboratory didn't do any work in taste. That could have been done in the other areas of the Research Center, but I don't have any knowledge of that.

Mr. WAXMAN. Prior to your employment at Philip Morris, what sort of scientific work had you done?

Mr. DENOBLE. I was working at the University of Minnesota, under a sponsorship of the National Institute of Drug Abuse. My work was with drug self-administration in non-human primates and rodents.

Mr. WAXMAN. You were doing animal tests on alcohol and barbiturates?

Mr. DENOBLE. That is correct, yes.

Mr. WAXMAN. OK. You were previously doing work on drugs for which there is a concern about both dependence and abuse?

Mr. DENOBLE. That's correct.

Mr. WAXMAN. And at Philip Morris you did similar types of animal research on nicotine, is that correct?

Mr. DENOBLE. Very similar, yes.

Mr. WAXMAN. Can you compare the tests you did on nicotine with the tests that the National Institute on Drug Abuse would do to determine if a drug has an abuse potential?

Mr. DENOBLE. Well, they are exactly the same tests. We did not do drug comparisons, but the test models are exactly the same.

Mr. WAXMAN. As I understand it, in order to test nicotine analogues, you had to understand the brain effects of nicotine itself. How did you approach this task? Where did you start?

Mr. DENOBLE. When the lab existed, we already had one test which identified whether rats could tell us whether they were given an injection of nicotine peripherally in the—systemically. Our first model, to get to a direct effect of the pleasurable effects, if you will, of nicotine, was to look at a self-administration model. That was the primary screen.

Mr. WAXMAN. I suppose that there are many brain effects that a substance might have, and many tests that could be done. It is my understanding that there are certain tests that qualify as hallmarks of potential drug abuse or addiction.

Am I correct that in the early 1980's, the three animal tests that would be done to identify whether a substance was potentially addictive would be self-administration, tolerance, and physical withdrawal?

Mr. DENOBLE. That is correct.

Mr. WAXMAN. And isn't it true that you did all these tests and that they were a central part of your work at the laboratory?

Mr. DENOBLE. That is also correct.

Mr. WAXMAN. Now, would you briefly describe for us how you tested for self-administration, tolerance, and physical dependence?

Mr. DENOBLE. Well, for self-administration, the animals were surgically prepared with a catheter that lodged itself just above the heart. The animals, after surgical recovery, could be hooked up to an infusion pump. If the animal pressed one of two levers, one lever didn't do anything, the other lever would deliver a nicotine solution into the vein.

If nicotine is a reinforcing agent, then the pressing of the lever would increase, and that is what we found. We did several manipulations and several investigations to clearly show that the animal was pressing the lever to obtain nicotine.

In terms of tolerance, a study design that Paul put together was to repeatedly inject animals with nicotine over several days, and then test to determine whether or not the animal was tolerant to the disruptive effects of nicotine.

When you inject nicotine in an animal and he is working on a lever for food, the performance of the animal becomes impaired. That performance impairment goes away as the animal has exposure to nicotine. We also demonstrated in that experiment that part of that tolerance was physiological and part of the tolerance was behavioral, that is, a learned tolerance.

In physical dependence, we conducted two large experiments in which we chronically administered nicotine to rats over several days, if not weeks. We challenged the nicotine in the animals with an antagonist, mecamylamine. Or in another experiment we let the—simply the nicotine, took it away from the animal. We did not observe any withdrawal syndrome as evidenced by changes in food-motivated behavior.

Mr. WAXMAN. So of the three hallmarks of dependence, you did find that there was self-administration and tolerance, but you did not find that there was a physical dependence?

Mr. DENOBLE. That is correct.

Mr. WAXMAN. OK. And did the studies that you did also indicate that nicotine has a potential for drug liability?

Mr. DENOBLE. Yes. The self-administration study is a classical hallmark to indicate that a solution or drug substance has a potential for abuse, yes.

Mr. WAXMAN. And what does "drug liability" mean?

Mr. DENOBLE. It essentially means that if you find it in an animal, it has the potential to be a drug of abuse in humans. You need to then go on to do other species, and other strains of animals, and also go into the human to determine the final factor.

Mr. WAXMAN. Now, on March 31, I released a version of your self-administration study. On that same day Philip Morris issued a statement, which I'd like entered into the record, without objection, as Exhibit 2.

RESPONSE OF PHILIP MORRIS U.S.A. TO CONGRESSMAN WAXMAN'S PRESS CONFERENCE

Dr. Victor DeNoble was employed by Philip Morris from April 1980 to March 1984 as a research scientist in the Research and Development Department. Dr. DeNoble conducted nicotine-related research and concluded that nicotine is a reinforcer in the class of nonaddictive chemical compounds such as saccharin, or water, and that he did not believe nicotine fit the accepted criteria for drug dependence. He also concluded that nicotine self-administration cannot be viewed as a form of drug "abuse" or as an "addiction."

Contrary to the suggestions that Dr. DeNoble's research has been somehow withheld from the scientific community and the public, we find dozens of publications authored by him, including five based on his nicotine-related research conducted while at Philip Morris.

At no time did Philip Morris seek an injunction, legal or otherwise, against the publication of any of Dr. DeNoble's research. As with virtually all industries, publication of research done while an employee must be reviewed and approved prior to such publication. We are aware of one instance when Dr. DeNoble failed to go through the Philip Morris manuscript review process and thus was told not to publish Philip Morris research until completing the process. An abstract based on that research was published.

Mr. WAXMAN. And they said, and I quote, "Dr. DeNoble concluded that nicotine self-administration cannot be viewed as a form of drug abuse."

On the basis of your work at Philip Morris, did you reach such a conclusion?

Mr. DENOBLE. No, sir, I did not.

Mr. WAXMAN. At this time, I'd like to show you Exhibit 3, which is a letter from Dr. Alan Leschner, director of the National Institute on Drug Abuse. That letter states that the findings in your study, quote, "indicate that nicotine has reinforcing properties, one of the hallmark characteristics of an addictive drug." Do you agree with that characterization of your work?

Mr. DENOBLE. Yes, I do.

[Exhibit No. 3 follows:]

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health

National Institute on Drug Abuse
5600 Fishers Lane
Rockville, Maryland 20857

(3)

APR 13 1994

The Honorable Henry A. Waxman
Chairman, Subcommittee on
Health and the Environment
Committee on Energy and Commerce
House of Representatives
Washington, D.C. 20515-6118

Dear Mr. Waxman:

I am writing in response to your request of April 11 for the evaluation by the National Institute on Drug Abuse (NIDA) of the significance of the findings presented in Dr. Victor DeNoble's 1983 research paper, "Nicotine as a Positive Reinforcer in Rats: Effects of Infusion Dose and Fixed Ratio Size." The findings from Dr. DeNoble's study demonstrate that nicotine does act in a reinforcing manner when tested in an animal model.

It is also important to note that the rate of nicotine self-administration varied with the dose of the drug. Furthermore, when the subject's baseline nicotine level was increased by the researcher, the rate of self-administration of nicotine by the subject in the study was decreased. These two findings support the contention that nicotine reinforcement was due to the pharmacologic effects of this substance. These findings from the DeNoble study indicate that nicotine has reinforcing properties, one of the hallmark characteristics of an addictive drug, and are consistent with those of NIDA-supported researchers who have studied the reinforcing effects of nicotine.

You also requested my comments on the statement by the Phillip Morris Company that the DeNoble study shows that "nicotine is a reinforcer in the class of nonaddictive chemical compounds such as saccharin or water." It is true that saccharin and water can also serve as reinforcers; however, the reinforcing properties of water depend upon the animals being deprived of water and the reinforcing properties of saccharin are due to its taste. In the DeNoble study, the animals were neither food nor water deprived, and nicotine was administered intravenously, which avoids taste effects. Therefore, nicotine does not have the same characteristics as water and saccharin.

I hope you will find this information helpful.

Sincerely,

Alan J. Leshner

Alan I. Leshner, Ph.D.
Director

Mr. WAXMAN. You were not able to show there is physical dependence. Am I correct that later studies did show a withdrawal syndrome in rats on nicotine, meeting the third criteria for addiction?

Mr. DENOBLE. That is correct. Those studies were not performed in our laboratory. They have since been performed between 1984 and 1994.

Mr. WAXMAN. Why did those studies reach a different result than yours?

Mr. DENOBLE. I have reviewed those studies, and the conclusion that I can come to is that those studies use very different measures than what we were using, much more sensitive measures than we were using. We modeled our dependence studies after work that I had done with alcohol and with barbiturates. So we didn't find it using those procedures, but other people have.

Mr. WAXMAN. I'd like to ask you about your study on self-administration. Prior to your work, had anyone ever shown that rats will self-administrate nicotine?

Mr. DENOBLE. There had been at least a half a dozen demonstrations that rats will self-administrate nicotine. The problem with most of those studies was that there was a confounding variable of inducement. It was not clear. You couldn't interpret clearly whether nicotine was a true reinforcing agent, or whether it was coupled to another thing going on in the animal's life.

Mr. WAXMAN. So your studies succeeded where others failed. Can you tell us why?

Mr. DENOBLE. I think the main difference between our study and previous studies was the infusion time. Back in the 1970's and 1980's, it was common to infuse a drug solution into the vein of an animal over a 13 to 15 second period. That's not what happens, if you observe a smoker.

A smoker takes smoke into his lung and nicotine is immediately going to the lung, and immediately getting to the brain. So we basically shortened our infusion times to less than 4 seconds, so that we were delivering a very quick, pulsed infusion. That seemed to be the critical factor in our success.

Mr. WAXMAN. I'd like to show you some posters, if we can have those displayed?

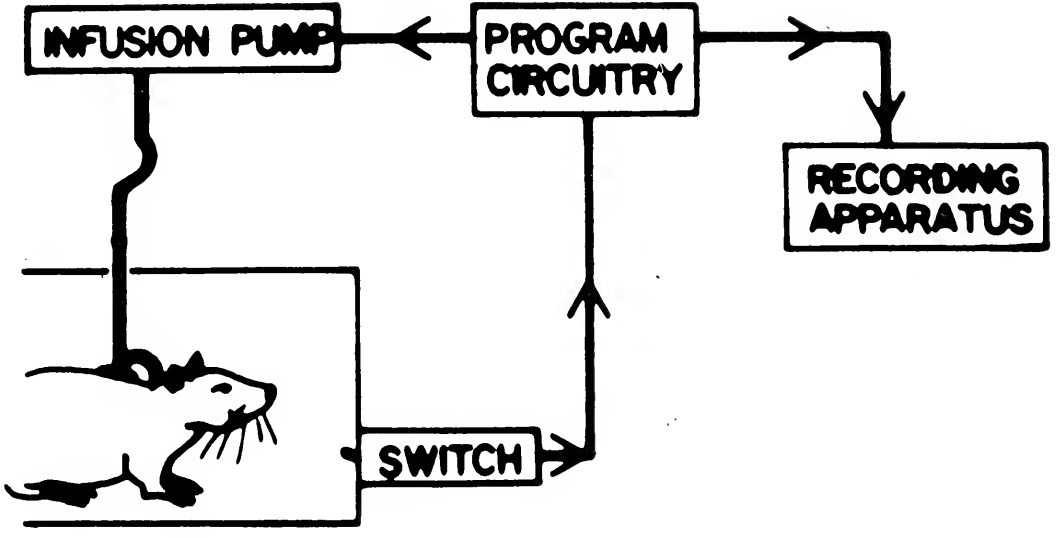
[Posters displayed.]

Mr. WAXMAN. The first one, Exhibit 4, is entitled, Self-administration Methodology. Could you explain it for us?

[Exhibit No. 4 follows:]

#4

SELF-ADMINISTRATION METHODOLOGY



Mr. DENOBLE. Yes. That is a poster, and this is a rat that would be inside of an experimental chamber and has a switch, what I refer to as a lever. The rat is also, you can see on his back he is surgically prepared with a catheter that lodges in his vein or the atrium of the heart. The rat has the option to go over and press the lever.

When he does, it activates some programming circuitry, you record when the press occurred. It also activates an infusion pump, and that pump then will infuse nicotine, or whatever solution you have, into the animal's vein. Again, if that solution is a reinforcer, the rat will continue to press the lever at reasonably high rates.

Mr. WAXMAN. We have another poster, which would be Exhibit 9.

That shows the number of times the rats press the lever for nicotine. Can you explain it for us? And let me indicate, by the way, that both of these posters are furnished to us from your slides that were given to us by you?

Mr. DENOBLE. That's correct.

This is a grouped data shot. Primarily, after the rats are surgically prepared with the catheter, you put them in the box and they are hooked up to a pump which has saline in it. And the animals don't press the lever very often for saline. If fact, they pressed it less than 12 times.

If you now substitute nicotine at a dose of 32 micrograms per kilograms, you can see that after several days an animal will inject itself well over—almost 90 times per 24-hour session. If you now remove the drug solution, in this case nicotine, the animal stops pressing the lever in a series of days. So the nicotine self-administration falls back down to the original saline levels.

Standard control is to reintroduce the nicotine. And that is the second large bar where you see it says "32." And that is, again, where the animals will resume pressing the lever, once nicotine is again made available intravenously.

Mr. WAXMAN. How did you pick the dose of nicotine to give to the rats?

Mr. DENOBLE. Well, we looked through the literature at the time, in the early 1980's. And it was determined by us that about 1 to 2 milligrams of nicotine was coming through in a cigarette. I just simply divided that by a 70 kilogram individual and came up with 30 micrograms per kilogram.

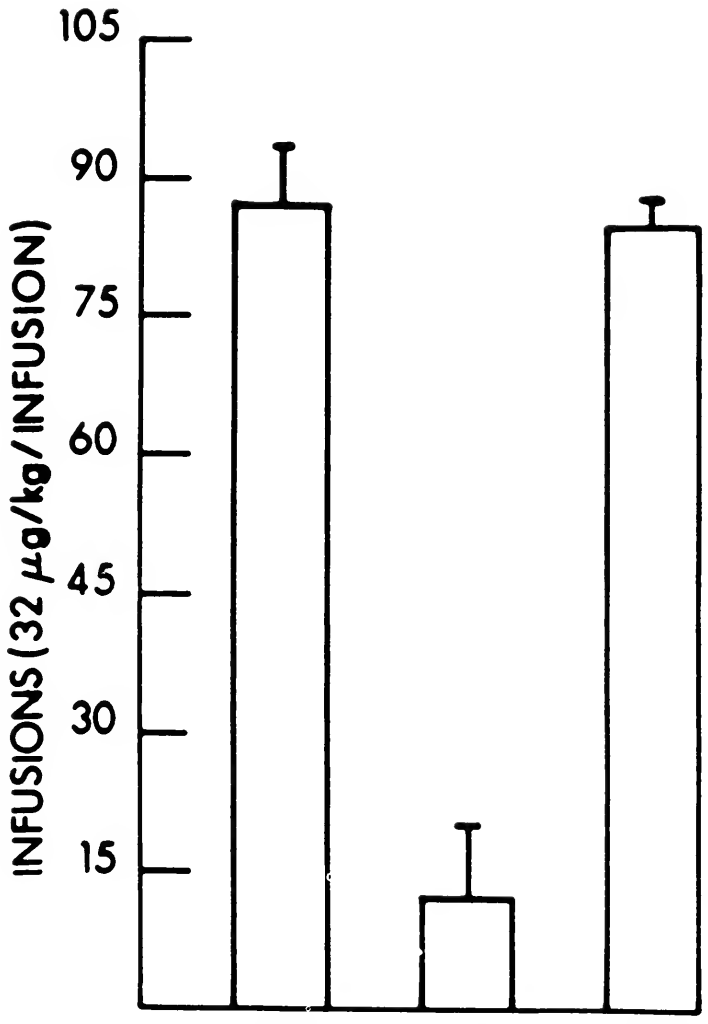
Mr. WAXMAN. And is that any relationship to what a human would get?

Mr. DENOBLE. It's basically—it's very difficult to answer that question. It's based upon what a single cigarette delivers to a human, but I don't know if it's any relationship to the physiological effects. I cannot answer that.

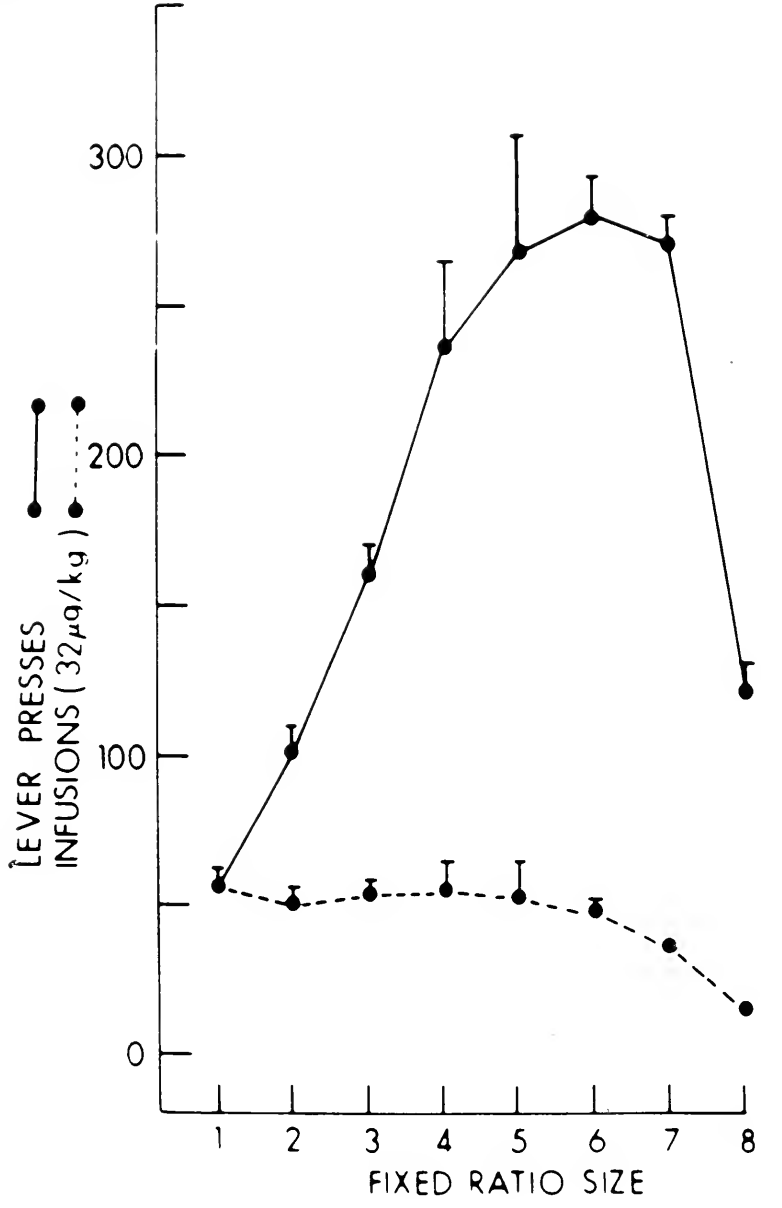
Mr. WAXMAN. We have the next exhibit, Exhibit 10. It's a little bit more complicated. It's my understanding that it shows how hard the rats will work for nicotine. Can you explain that to us?

[Exhibits 9 and 10 follow:]

#9


105
90
75
60
45
30
15
INFUSIONS (32 µg/kg/INFUSION)
32
0
32
NICOTINE DOSE (µg/kg)

#10


LEVER PRESSES
INFUSIONS (32μg/kg)
300
200
100
0
1
2
3
4
5
6
7
8
FIXED RATIO SIZE

Mr. DENOBLE. Can I walk over there, or is that hard to do?

Mr. WAXMAN. That's going to be a little difficult to get this on the microphone.

Mr. DENOBLE. That would be fine.

If you look at what's called fixed ratio size, that is how many times a rat has to press a lever. And if you look at the unit number 1, he gets a single press, he gets a single injection. If you now say to the animal, I'm going to see how hard you'll work for it, I'm going to ask you to press the lever twice. The animal——

Mr. DENOBLE. Thank you. This represents an animal pressing the lever twice for nicotine. What is interesting is this dotted line tells you how many infusions the animal is taking. Here he is taking a stable level of infusions, if you ask him to double his work output.

You can ask him to triple it, quadruple it, et cetera. The animals will continue to work and press the lever to get nicotine, up to about a fixed ratio of about 6 or 7, and then it begins to fall off. The cost is just too high.

Two points about this slide. One is, animals will work for nicotine; and second is, animals will maintain a constant level of nicotine infusion over different work schedules.

Mr. WAXMAN. At our April 14th hearing, Philip Morris' chief executive officer testified that you had, quote, "Concluded that nicotine is a reinforcer in the class of non-addictive chemical compounds such as saccharine and water." We asked Philip Morris for these and other relevant documents, but they were unable to provide them prior to this hearing.

Is Philip Morris correct that you concluded after you did this work, that nicotine is a reinforcer comparable to saccharine and water?

Mr. DENOBLE. No, not at all.

Mr. WAXMAN. What would be the difference?

Mr. DENOBLE. Well, water is a reinforcer, but you need to be food-deprived or very nervous to drink it. Food is a reinforcing agent, but you need to be hungry, or it needs to taste good, it requires tongue.

Nicotine was being injected directly into the vein. We went on to use a series of blocking agents to show that it was the brain activity of nicotine, not its effect on the periphery, not its effect on taste systems, that would determine its reinforcing effects. An animal doesn't have to need nicotine for it to be a reinforcer. All it has to do is experience it.

Mr. WAXMAN. Now, you said, "food." Would that also apply to saccharine, that you need the taste of the saccharine?

Mr. DENOBLE. Exactly. Yes, the reinforcing effects of saccharine are clearly mediated via its interactions with the taste system in the mouth.

Mr. WAXMAN. Now, if you ran the kind of tests you did for nicotine on saccharine, what would you find?

Mr. DENOBLE. Saccharine is not self-administrated intravenously, to the best of my knowledge.

Mr. WAXMAN. So you have an intravenous feeding of this nicotine that's going right to the brain. If you put saccharine intravenously,

there would be no taste, there would be no reason why they would want to go back to it?

Mr. DENOBLE. I don't know of any experiment that has ever demonstrated that, no.

Mr. WAXMAN. Finally, I want to ask you about a statement in the 1983 version of your unpublished article on self-administration that doesn't appear in your 1986 version. In the 1983 version of the article, you state that nicotine "May be a weak reinforcing agent." What was the basis for this statement, and why did you take it out in the later version of the article?

Mr. DENOBLE. In the earlier version of the article, I was doing some literature comparisons between nicotine and other intravenously delivered reinforcers, specifically, psychostimulants like cocaine and amphetamine. And if you look at just how hard an animal will work for these substances, nicotine looks like a weak reinforcer. And I had made that statement that I thought that was a fair assessment at that time.

As we began to think and know more about the reinforcing effects of these drugs, we also found that rat models do not necessarily predict how reinforcing something will be in a human. For example, alcohol is not a very good intravenously delivered reinforcer in rats. But alcohol is a very powerful reinforcing agent in humans. So I did not put that in the second article, simply because I didn't think my data was strong enough to make that statement.

Mr. WAXMAN. Put this all in a historical context for us. Your work on nicotine at Philip Morris, what significance did it have at that time frame, and how should we view this research project?

Mr. DENOBLE. The work that we did with nicotine was clearly some years ahead of the external scientific community. It wasn't until 1989 that Bill Corgal demonstrated that nicotine would function as an intravenously delivered reinforcer for rats using the same models that I used, that Paul and I used.

Interestingly enough, he found the same dosing schedules to be effective. The work that we did on self-administration, on dependence, on tolerance, on frustration, clearly would have moved the scientific community much further than it had been moved by that work not getting out.

Mr. WAXMAN. Dr. Mele, do you want to add anything to this?

Mr. MELE. Just that this work, some of these studies were the first to be done with nicotine. I have no doubt that other people would have performed these studies subsequently, just as has been done recently in Toronto, but they weren't being done at the time.

And to quote a recent review article in Science, a news story, it said that, basically, it took 6 or 7 years for the nicotine self-administration model to be developed and come out, whereas, it would have been out much earlier had this work been allowed to go out and stay out.

Mr. WAXMAN. So your work at Philip Morris indicated the reinforcing nature of nicotine, information that didn't come out until years later and led to the Surgeon General's Report, I guess it was 1988 or 1989, where the public was finally informed by the chief medical officer of this country that nicotine is an addictive substance in cigarettes.

Mr. DENOBLE. That's correct. I think the significance of the self-administration is only—is in part because it was a rat model. And if you can understand the biochemistry of this system, if you can understand how drugs interact in the brain, you need to run dozens if not hundreds of animals. So the significance—other people had already been doing this from 1984 on, but the rat model wasn't developed until 1989.

Mr. WAXMAN. Thank you very much. Mr. Bliley?

Mr. BLILEY. Thank you, Mr. Chairman. Dr. DeNoble, Dr. Henningfield and the Surgeon General have testified before this subcommittee that nicotine use creates a physiological dependence. They have testified that such dependence is important because it shows that nicotine use is addicting. Isn't it true that while you were working at Philip Morris, you told your superiors that your experiments showed that nicotine use does not create a physiological dependence?

Mr. DENOBLE. That's true. We demonstrated that in at least two separate experiments.

Mr. BLILEY. Thank you. Dr. Henningfield works at the National Institute on Drug Abuse. In 1979, NIDA published a report titled, "National Institute on Drug Abuse Technical Review on Cigarette Smoking As An Addiction." Isn't it true that while you were employed at Philip Morris, you reported to your superiors that most of the evidence in this report was, quote, "Fancy", rather than fact? And that, in fact, NIDA had chosen the researchers used in this report in a biased way so that NIDA could claim publicly that cigarette smoking was an addiction?

Mr. DENOBLE. I don't know that I said that. If I could get a—it's very possible that I reviewed those documents, but I don't know that those are my words.

Mr. BLILEY. After this report by the NIDA came out, you did your experiments in which you carefully examined whether or not nicotine use created a physiological dependence, and you found that nicotine use did not create a physiological dependence? You then reported this to Philip Morris?

Mr. DENOBLE. That's correct. The models we used were at the time, in the 1980's, were excellent models. The animals are very highly motivated in these models. And the animals clearly would show a physical dependence to things like alcohol and barbiturates. But we did not find it with nicotine.

Mr. BLILEY. You also did experiments while at Philip Morris to determine if—and I'll try this word—acetaldehyde use caused physiological dependence, and you found that acetaldehyde use did not create a physiological dependence?

Mr. DENOBLE. Yes. We used the same experiments that we did with nicotine.

Mr. BLILEY. You also did experiments while at Philip Morris to determine whether injections of acetaldehyde and nicotine mixed together caused physiological dependence. And you found that acetaldehyde and nicotine mixed together did not cause a physiological dependence?

Mr. DENOBLE. That is correct.

Mr. BLILEY. We have been told by other witnesses that because animals will self-administer nicotine, this is proof that nicotine is

addictive. Isn't it true that while you were working at Philip Morris, you told your superiors that animals will self-administer saccharine?

Mr. DENOBLE. No, sir. I never said that they will self-administer saccharine. They will work for saccharine. You can press the lever and get a food pellet or get saccharine, and that is a self-administration procedure. The difference between self-administration of saccharine and food and nicotine is that one is delivered intravenously, the other one goes through the peripheral system. So, saccharine, yes, you can self-administer it but only through the oral route. It will not go intravenously.

Mr. BLILEY. Isn't it true that you conclude from your research at Philip Morris that behavioral factors are primarily responsible for tolerance of nicotine?

Mr. DENOBLE. No. I'd like to defer that to Dr. Mele. Paul was an expert, is an expert in tolerance and nicotine.

Mr. MELE. Well, I ran the tolerance studies anyway. Yes, we did determine that under certain conditions behavioral factors contributed heavily to the development of tolerance to nicotine. Behavioral factors were not the only component, at least back then, what was termed a physiological or metabolic component. There was a duel role in our studies, at least in the first studies we ran, the behavioral component was much larger.

Mr. BLILEY. And you reported this to your superiors at Philip Morris, both of you?

Mr. MELE. Yes.

Mr. DENOBLE. Yes.

Mr. BLILEY. Isn't it true that you also concluded from your research at Philip Morris that if there is a physiological tolerance to nicotine, it is like that developed to that of saccharine or caffeine?

Mr. MELE. I don't know that tolerance develops to saccharine. I do know that tolerance develops to caffeine, yes.

Mr. BLILEY. And you reported that to your superiors?

Mr. MELE. Tolerance to saccharine—I'm sorry, tolerance to caffeine, tolerance to nicotine, tolerance to alcohol, pentobarbital, it's pretty much the same. Different mechanisms perhaps, physiological mechanisms in the liver, but the general conditions are the same, yes.

Mr. BLILEY. This subcommittee had been told by some witnesses that the evidence is clear that nicotine alone is an addicting substance, in part because ceasing the use of nicotine causes physiological withdrawal symptoms. Isn't it true that while you were employed at Philip Morris, you told your superiors that your research showed that stopping nicotine use does not result in physiological withdrawal?

Mr. MELE. In rats, yes.

Mr. BLILEY. While you were employed at Philip Morris, you also did experiments to determine if stopping acetaldehyde use caused physiological withdrawal symptoms. And while you were working at Philip Morris, you told your superiors that your experiments found no physiological withdrawal resulted from stopping the use of acetaldehyde, isn't that correct?

Mr. MELE. Yes. In our experiments in rats.

Mr. BLILEY. While you were working at Philip Morris, you also did experiments to determine if stopping the use of acetaldehyde and nicotine mixed together caused physiological withdrawal symptoms. Again, while you were employed at Philip Morris, did you not tell your superiors that your experiments showed that stopping the use for acetaldehyde and nicotine mixed together did not cause physiological withdrawal?

Mr. MELE. Yes, we did.

Mr. BLILEY. Am I correct that all of your experiments at Philip Morris were with rats, and that none of your experiments involved people?

Mr. MELE. That is correct.

Mr. BLILEY. Doctor, 40 million Americans have quit smoking. Isn't it true that while you were working at Philip Morris, you advised your superiors that the relative ease with which people can stop smoking without formal treatment identifies smoking behavior as fundamentally different from addictive behavior?

Mr. MELE. It's not fundamentally different, but it clearly is different than if you are an alcohol, or if you are a heroin abuser, that is correct.

Mr. BLILEY. Well, is that what you advised your superiors?

Mr. MELE. Yes, that's true.

Mr. BLILEY. Am I correct that acetaldehyde is something that results naturally from burning tobacco?

Mr. MELE. That is, yes, correct.

Mr. BLILEY. Nicotine, of course, is also a natural part of tobacco, isn't it?

Mr. MELE. Yes, it is.

Mr. BLILEY. Dr. DeNoble, I now want to ask you about your research paper on rats' self-administration of nicotine that was submitted to Psychopharmacology and withdrawn. As I recall, the title of that paper was, quote, "Nicotine as a Positive Reinforcer in Rats, Effects of Infusion Dose and Fixed Ratio Size."

According to both the abstract and the first page of your manuscript your research found that "even determination of prolonged access to nicotine, under which it functions as a positive reinforcer, does not result in physiological dependence," unquote. Is that right?

Mr. DENOBLE. That is a correct observation, yes.

Mr. BLILEY. The amount of nicotine injected directly into the rats' veins, in this experiment, were much higher than the amount of nicotine a smoker receives, isn't that true?

Mr. DENOBLE. The amount of nicotine injected at the 32 microgram dose is roughly the equivalent of one cigarette. But what we did was we did a spread of ranges of doses, so we showed a 32, 16, 8, and 4. Eight and four were not as reinforcing as 16. So we did branch the range. So it is roughly the equivalent of a single cigarette, or less, in a rat. I also might add, sir, that animals have been shown to be either more sensitive to drugs, depending upon the drug class. So it's very difficult to make a direct comparison to the human.

Mr. BLILEY. You reported, I believe, in this paper, as you told your superiors all the time that you were employed at Philip Mor-

ris, that there was no evidence of physiological dependence to nicotine in the experiment. Is that true?

Mr. DENOBLE. That is correct, yes. We were unable to find it using a model in which an animal is a highly motivated animal. The model is, you deprive the animal of food, and the animal has to work for food, and then you have it being administered nicotine.

Pull the nicotine away, and the animal—your evidence of physiological dependence is that the food-directed behavior is changed in some way, is altered. We did not observe that. We did not see an animal sort of show a physical dependence withdrawal syndrome in that particular model.

Mr. BLILEY. This subcommittee has been told that the evidence has been clear for some time that nicotine itself is an addicting substance, that the use of nicotine alone creates a physiological dependence, and that stopping only the use of nicotine causes physiological withdrawal symptoms. Isn't it true that while you were employed by Philip Morris, you told your superiors that your research at Philip Morris showed that nicotine does not create a physiological dependence, and that stopping the use of nicotine does not create physiological withdrawal?

Mr. DENOBLE. Yes, we did. In the same way we also said to them that self-administration in the rat does not necessarily predict the amount of self-administration in the human. Gentlemen, you have to be very careful about predicting from rats to humans.

What the animal data shows you is that there is something to look at. And when you see self-administration, you need to go further. When you fail to find physical dependence, you need to go further to determine whether it's really going to be generalizable to the population.

Mr. BLILEY. Mr. Chairman, I assume I'll be allowed to go on?

Doctor, isn't it true that to your knowledge Philip Morris never used any of your research to change the acetaldehyde or nicotine content in any commercial cigarette?

Mr. DENOBLE. Yes. I have no knowledge of that.

Mr. BLILEY. Isn't it true that to your knowledge, Philip Morris never used your research to create a new commercial cigarette

Mr. DENOBLE. That is correct.

Mr. BLILEY. Dr. Mele, if I might, isn't it true that while you were working at Philip Morris, you advised your superiors that your experiments showed that nicotine use does not create a physiological dependence?

Mr. MELE. No, I don't recall that at all.

Mr. BLILEY. You didn't——

Mr. MELE. Only as part of, possibly, a co-author on Dr. DeNoble's—I know the tolerance work I was working on that involved chronic administration took—for over 100 days, we did not find a physiological dependence in that study. But I don't recall specifically discussing that with anybody at Philip Morris. It may be in the main script, it may not. I just don't recall that.

Mr. BLILEY. Isn't it true that while you were employed at Philip Morris, you advised your superiors that your experiments showed that acetaldehyde use does not create a physiological dependence?

Mr. MELE. Yes. Under the conditions which we ran the studies, which were very limited, we did not find a physiological dependence.

Mr. BLILEY. Isn't it true that while you were employed at Philip Morris, you also did experiments to determine if discontinuing the use of nicotine or acetaldehyde created physiological withdrawal symptoms, and that you told your superiors at Philip Morris that your research showed that discontinuation of nicotine or acetaldehyde did not cause physiological withdrawal symptoms?

Mr. MELE. Yes. Again, under the conditions of those experiments, we could not identify any physiological withdrawal.

Mr. BLILEY. And you did all of your experiments, of course with Dr. DeNoble, were with rats?

Mr. MELE. Correct.

Mr. BLILEY. Isn't it true that some rats in your experiments at Philip Morris like nicotine more than other rats?

Mr. MELE. Some rats may administer higher doses, or have different dose response curves than other rats. That is very typical of any drug effect in any rat or any animal. There are individual differences.

Mr. BLILEY. Isn't it true that albino rats did not seem to like nicotine as much as hooded rats?

Mr. MELE. I didn't work with albino rats at all when I was at Philip Morris.

Mr. BLILEY. Though you didn't work with albino rats, isn't it generally true that albino rats don't seem to like nicotine as much, Dr. DeNoble?

Mr. MELE. I'm not sure. I can't answer that question.

Mr. DENOBLE. I can't answer that question either. I'm not sure where that data is coming from.

Mr. BLILEY. Well, isn't it true, Dr. DeNoble, that you decided to use hooded rats in your experiments because hooded rats were easier to get to self-administer?

Mr. DENOBLE. No. That's incorrect. There was a paper published in the early 1980's, I believe, around 1980 actually, which demonstrated that the albino rat was not a prototypical animal to do drug research because it had altered biochemistry, because it is an albino.

The hooded rat has an intact, more generalizable biochemistry in the brain, so that a hooded rat's biochemistry is much closer to that of a monkey's, and it's closer to that of a human. So we elected to do all of our studies in hooded rats, whether it be self-administration, tolerance, dependence, because their brain biochemistry represented more what a normal animal is.

Mr. BLILEY. Thank you. Thank you, Dr. DeNoble. Thank you, Mr. Chairman.

Mr. WAXMAN. Thank you, Mr. Bliley. Mr. Synar?

Mr. SYNAR. Thank you, Mr. Chairman. First of all, believe it or not, I think Mr. Waxman, Mr. Wyden, and I understand why the executives of these seven major tobacco companies came in here a couple of weeks back, and in the face of overwhelming historical medical evidence, denied the addictiveness of nicotine. They have been counseled by their attorneys that an admission on their part would increase their chances of liability.

Dr. DeNoble, you don't have that same responsibility; you are a scientist. And I want to ask you, do you agree with the statement we heard from the executives under oath, that nicotine is not addictive?

Mr. DENOBLE. I'll answer that in 1994, not 1984. I think there is an overwhelming body of evidence that nicotine does produce an addiction in the human. That overwhelming body of evidence does not come from my single rat study or Paul's study on tolerance. So my opinion in 1994 is, yes. I think in 1980, 1981, 1982, 1983, and 1984, I think there were some doubts in my mind because the data wasn't there.

Mr. SYNAR. So what you are saying is that your study didn't definitively prove that nicotine was addictive. But it predicted that this was a serious problem, as you had seen, and therefore occasioned further study and review? Is that basically what you are saying today?

Mr. DENOBLE. It certainly did indicate that nicotine had an abuse liability and we needed to look further to determine other factors, yes.

Mr. SYNAR. Mr. Johnson, the chairman of RJR, during his testimony a couple of weeks back, said that nicotine is comparable to saccharine and chocolate. Your study doesn't support that proposition, does it?

Mr. DENOBLE. No, sir, it does not.

Mr. SYNAR. In fact, that's stretching the truth a little bit to say that we could compare nicotine to saccharine and chocolate?

Mr. DENOBLE. Experimentally, scientifically, I believe that to be correct, yes.

Mr. SYNAR. You've testified this morning, Dr. DeNoble, that one purpose of the analogue research study was to find a synthetic form of nicotine with reduced cardiovascular effects. Why were your superiors at Philip Morris concerned about the cardiovascular effect of nicotine?

Mr. DENOBLE. That program actually was in existence before I got to Philip Morris. The nicotine analogue program I know was there before I got there because the analogues were there, and they also had some animal experiments ongoing.

The discussions around nicotine in the 1980's—in the late 1970's, early 1980's was that there was a cardiovascular risk. Clearly, nicotine has effects on the cardiovascular system. It was also clear that effect on the cardiovascular system could be related to increased heart disease.

So the objective of the program was to come up with a molecule that would mimic nicotine's effect in the brain, and would not affect the peripheral nervous system and therefore not have cardiovascular liability.

Mr. SYNAR. So beyond addictiveness, nicotine has other consequences with respect to the health of a person?

Mr. DENOBLE. Yes.

Mr. SYNAR. Dr. DeNoble, could you outline the official policy at Philip Morris with respect to documentation of studies? What I'm interested in is how were the original papers that you worked on archived? How were the documents maintained? Where were they

kept? Was there periodic destruction of those documents? Is there a master index of those studies and working papers?

Mr. DENOBLE. The laboratory would write annual reports every year. They were fairly extensive. Paul and I would put them together. All data, all original data would be archived in an annual report and sent to—would be distributed throughout the research center and then sent to central file. We kept all our original data in notebooks which would also go to a central filing unit.

I know of no instance in which data had been destroyed, at least not while I was there, up until April of 1984. We also gave interim reports which would be considered pharmacology reports, or, were we to publish—try to write a manuscript, that manuscript would also be distributed throughout the research center.

Mr. SYNAR. Now, did any other researchers at Philip Morris conduct research on humans while you were there?

Mr. DENOBLE. On humans?

Mr. SYNAR. On humans.

Mr. DENOBLE. Yes. There was one laboratory that conducted electrophysiological studies in humans, looking at the effects of cigarette smoke on electrical brain activity, and also looking at the effect of flavorants added to the nasal cavity, and looking at the effects on brain activity.

Mr. SYNAR. OK. Let's talk about the article which has been really the focus of the controversy. Did Philip Morris orally request that you pull your article from the magazine, or did they send you correspondence requesting that?

Mr. DENOBLE. I never received a correspondence. I just was asked to remove it by our manager. We tried very hard to convince him that we shouldn't remove it from publication, but we lost that battle, so we were told to pull it from the journal.

I immediately called Herb, Herb Barry, up and told him of the situation and sent him off a note, as an official record, that we needed to withdraw the paper.

Mr. SYNAR. OK. Just for the record, Dr. DeNoble, once again, why did you leave Philip Morris?

Mr. DENOBLE. I left because the lab was closed down. It was abruptly closed down in April of 1984.

Mr. SYNAR. Did they give you a reason that they couldn't find another position for you?

Mr. DENOBLE. Actually they never said that they couldn't. They just said that it would never be to the caliber of the position that we had, that clearly it would be a step down in pay as well as visibility. I think that clearly we needed to leave.

Mr. SYNAR. Did you look for other jobs in the tobacco industry?

Mr. DENOBLE. No. We're not allowed to do that. Part of your contractual agreement with Philip Morris is that you cannot work for a competitor. And I don't remember the time frame, and I think it was 7 years or something like that.

Mr. SYNAR. OK. Thank you, Mr. Chairman.

Mr. WAXMAN. Thank you, Mr. Synar. Mr. Greenwood?

Mr. GREENWOOD. Thank you, Mr. Chairman. Back to the purpose of this study. Congressman Synar mentioned that in your testimony you referenced the goal of this program was to identify a nicotine analogue that would have central nervous system effects

without effects on the cardiovascular system. We understand that now.

First of all, let me ask you this. Has such an analogue ever been discovered, to your knowledge?

Mr. DENOBLE. We did discover a lead series of analogues which had met the criteria of reduced cardiovascular effect and maintained the brain effects. So, yes, we were able to identify at least two analogues that would meet that criteria.

Mr. GREENWOOD. So what are the practical implications of that and what uses have been made, if any, to your knowledge, of these analogues?

Mr. DENOBLE. I don't think any use has been made of it. In fact, it was basically put on the shelf. There was not, to my knowledge, any activity around these analogues.

Mr. GREENWOOD. Are these analogues found in nature or are they synthetic?

Mr. DENOBLE. They are synthetic. They are organically synthesized.

Mr. GREENWOOD. Was the goal to somehow remove the nicotine from tobacco and substitute this synthetic analogue?

Mr. DENOBLE. That was exactly the goal, to remove nicotine from the tobacco and have the analogue be a substitute so that you would produce a safer cigarette.

Mr. GREENWOOD. Is the idea for the analogue that you were searching for and that you say has been found, to have the same habit-forming qualities of nicotine without the health risks?

Mr. DENOBLE. That's a very difficult question to answer, when you talk about habit forming. If you are asking me, would it maintain self-administration, would it act as a reinforcing agent, would it maintain the brain receptor qualities, the answer to that is, yes, that is correct.

Mr. GREENWOOD. Do you have any information as to why, if that synthetic analogue has been discovered, it hasn't been utilized in the production of tobacco products?

Mr. DENOBLE. No, I don't. But I would also mention that the analogue that I'm talking about, or the series of analogues, meets the criteria. But before you could actually use that, you would have to go through a whole series of other testing, and that was never done.

Mr. GREENWOOD. Would it have to be approved by the FDA?

Mr. DENOBLE. I guess that would depend upon how you put it in tobacco. You could, theoretically, genetically engineer plants to grow it, if it's a simple molecule. But that's far beyond my expertise.

Mr. GREENWOOD. Were you asked to devise the format of this research, or were you directed by superiors at Philip Morris as to how your research was to be conducted?

Mr. DENOBLE. No. The goals of the laboratory were pretty straightforward. It was an analogue program. We put together the screening procedures. With the exception of the drug discrimination procedure which was there, we determined the direction of the lab in collaboration with management. I met with my manager weekly to discuss research directions and data. So it was really a collabo-

rative arrangement. The people in Richmond are good scientists, and it was a good exchange of ideas.

Mr. GREENWOOD. Now, if I understand your testimony, the reason that we've heard very different kinds of answers to different questions directed by different members of the panel is that when Chairman Waxman or Mr. Synar have asked you questions about the addictive quality or the reinforcing qualities of nicotine, you have really relied on the information that has been brought forward by other researchers in the past 10 years.

When you've been asked to give information based your own study of 10 years ago, you had different information. So, on the one hand, you said, yes, my study didn't demonstrate that nicotine was addictive or reinforcing, however, we now know that it's the case. Does that correctly summarize what you said?

Mr. DENOBLE. Let me see if I can clarify it. The work that was done in 1981, 1982, and 1983, on nicotine self-administration clearly shows that nicotine is an intravenously driven reinforcer. That is a characteristic of a drug of abuse.

When you talk about addiction, you are talking about a human condition. Rats—we can't predict that nicotine is addictive in humans based upon that single observation in rats. So my study stands, our study stands, as this is a characteristic of the drug, it's definitely a substance that could have an abuse liability. That ends right there.

From 1984 on, there have been numerous studies demonstrating in humans, as well as in monkeys, that nicotine has qualities that the committee calls addicting.

Mr. GREENWOOD. Now, we talked about other substances throughout these hearings, everything from saccharine and caffeine to alcohol and amphetamines to heroin. Is it possible to place the qualities of nicotine on some sort of a spectrum? Is it more like caffeine or is it more like heroin, in terms of its effect on either mice or humans?

Mr. DENOBLE. Well, in humans I think the data indicates that it's more like cocaine and amphetamine. Those are the studies that have been done back in the late 1980's. In the animal, you have to do direct comparisons, and very few of those studies have been done. In the rat, nicotine is probably like alcohol, if you want to talk about weak reinforcing effects. But in the human, I think the data indicates it's more like a stimulant.

Mr. GREENWOOD. Caffeine is a stimulant, right?

Mr. DENOBLE. Caffeine, I think, is classified as a weak stimulant, yes.

Mr. GREENWOOD. A weak stimulant. So you are saying it's more like cocaine than it is like caffeine?

Mr. DENOBLE. That would be the data, that is the research, yes.

Mr. GREENWOOD. OK. There are lots of pleasurable responses that you can get both rats and humans to work for, to push pedals for, or whatever else they do. What is the difference between that and addictive behavior?

Mr. DENOBLE. Not much. The difference is that the animal is in a controlled experimental procedure, and you are controlling variables. When a human self-administers a drug, it's the same situation. The human has to go buy it, he has to work to get it. I mean,

the comparisons, the similarities are astounding, so they are very similar. Self-administration techniques predict what humans will do.

Mr. GREENWOOD. There has been probably too much made about the food comparisons to cigarettes. But there are people with eating disorders who seem by a lot of measures to be as addicted to foods as people are to substances. Are we talking about the same range of human behavior?

Mr. DENOBLE. Not really, because things like bulimia or people who have food addictions, may, in fact, be driven by biochemical imbalances in the brain. That may, in fact, be a psychiatric disorder. You don't have to have a psychiatric disorder to be addicted. The addiction or the self-administration is cued by the drug in the brain, so they are really very different things.

Mr. GREENWOOD. OK. Finally, your testimony in this hearing has been fascinating in terms of science. It is interesting to learn about your experiments, the experiments that have followed, and the various qualities that are found in nicotine. But we are here to make public policy. So I guess I have to ask you this: What are you here to tell us in terms of public policy? This is very interesting science, but what should we take from your testimony? What do you want us to do in response to your testimony, in terms of crafting public policy?

Mr. DENOBLE. Well, I'm not here to make public policy. I'm here to tell you of the science that was done between 1980 and 1984. I'm here to position that science as to its relevancy with reference to other science that's being done from 1984 on. I'm not going to be so bold as to tell you what to do with public policy. I can't do that.

Mr. GREENWOOD. Thank you, Mr. Chairman.

Mr. WAXMAN. Thank you, Mr. Greenwood. Mr. Wyden?

Mr. WYDEN. Thank you, Mr. Chairman. Let me, if I could, Dr. DeNoble, go back to this point with Mr. Bliley, because Mr. Bliley was talking specifically about nicotine effects and showing withdrawal in rats. Now, you testified that subsequent studies show that nicotine does cause withdrawal in rats. What was it about these studies that made it possible to identify withdrawal symptoms?

Mr. DENOBLE. Our study, as I mentioned, relied upon a very strongly motivated behavior. If the rat didn't press the lever, it didn't eat. And that is a very strong drive. These later studies used very subtle measures. Whereas a rat doesn't necessarily have to press the lever to eat, but maybe to deliver itself a glucose sweetened solution. So it's a reward, if you will, a candy.

Under those conditions where the rat is not so strongly motivated, people have shown that nicotine will disrupt those measures. So the difference was that ours was a very highly motivated animal. If you don't press, you don't eat. The other one is, if you don't press, well, maybe you don't get your glucose.

Mr. WYDEN. Let me turn now to an area that Chairman Waxman, I think, has really focused on very correctly, and that is this matter of secrecy in the tobacco industry. I just look at the events of what went on in your situation, and many others, as just sort of like a spy novel, with all this cloak-and-dagger kind of activity.

I wanted to ask you about some of the details of your situation. When you were hired in 1980, did you discuss whether you would be able to publish the results of your research at Philip Morris?

Mr. DENOBLE. Yes, I did. And, as with most companies, it clearly depended upon the proprietary position. I do—when I went there it was clear to me that I would not be able to publish everything when I wanted to, but eventually we thought we'd be able to publish everything. So, yes, they were very clear on that.

Mr. WYDEN. Did Philip Morris try to keep your work secret?

Mr. DENOBLE. During the first 2 years of the laboratory's existence, the lab was really quite secretive. The animals would be brought in at night or in very early morning, under a cover so that—people knew that we had animals in the building. They couldn't not know, but they didn't know what we were doing with them. And we weren't permitted to discuss our research at any of the research meetings for the first 2 years or so.

Mr. WYDEN. So the animals were brought in and they were covered up?

Mr. DENOBLE. Yes. That's correct.

Mr. WYDEN. And when the rats had died, were they taken out after hours, and that sort of thing?

Mr. DENOBLE. Usually they were incinerated, yes.

Mr. WYDEN. And nobody was allowed into the laboratory without management's permission?

Mr. DENOBLE. That is correct.

Mr. WYDEN. What would you say if another scientist working in the building asked you about your work?

Mr. DENOBLE. We used to tell them we were just doing some experiments in the nicotine analogue program. Everybody knew about the analogue program, but the animal research was not a very well-known commodity.

Mr. WYDEN. Who told you to follow all these secrecy procedures?

Mr. DENOBLE. They were laid out to us by our management when I was hired.

Mr. WYDEN. And that was Mr. Dunn and——

Mr. DENOBLE. Dr. Dunn, Dr. Osdene.

Mr. WYDEN. Now, in the fall of 1982, as I understand it, you submitted a manuscript to Philip Morris on the self-administration matter. You wanted permission to publish the paper. We can give you that exhibit. Who reviewed this paper and whether approval was given?

[Testimony resumes on p. 49.]

[Exhibit 11 follows:]

EXHIBIT

From: Henningfield file provided as a draft prior to or at the time of submission for publication. Unpublished

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NICOTINE AS A POSITIVE REINFORCER FOR RATS: EFFECTS OF INFUSION DOSE AND FIXED RATIO SIZE

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ABSTRACT

Lever pressing by rats was established and maintained by intravenous nicotine infusions. The rate of lever pressing was reduced by substituting saline for nicotine infusions or by giving the rats response independent nicotine infusions. The rate of lever pressing was sensitive to both dose and fixed-ratio size. These results show that nicotine can function as a positive reinforcer for rats in the absence of other inducement or weight reduction procedures. In addition, the present results extended previous work showing that termination of prolonged exposure to nicotine does not result in a physiological dependence.

Nicotine is one of the most widely used compounds, however, it is only recently that the effects of nicotine on schedule-controlled behavior have been systematically studied (1,2). In rats, nicotine increases responding maintained under fixed-interval (FI), variable-interval and differential-reinforcement of low rate schedules of food or water presentation and under schedules of electrical shock postponement (1). Nicotine decreases responding under fixed ratio (FR) schedules of food or water presentation. Qualitatively similar results on responding have been reported in squirrel monkeys maintained under a multiple FI-FR schedule of either presentation of food or termination of a stimulus associated with electric shock (2). In addition it has been shown that intravenous injections of nicotine will maintain high rates of lever-pressing by squirrel monkeys under a second order schedule. Under this schedule responding results in the presentation of a visual stimulus that is intermittently associated with response contingent nicotine injections.(3)

Many compounds from different pharmacological classes can increase and maintain behavior that leads to self-administration of those compounds (4). However,there is little evidence that rats will intravenously self-administer nicotine unless self-administration is induced by a food delivery schedule (5) or they are given programmed nicotine infusions for several days (6). The levels of responding maintained by intravenous nicotine following programmed infusions have been low (6). The present study demonstrates that intravenously delivered nicotine functions as a positive reinforcer in the absence of food inducement or programmed infusion conditions. Nicotine self-administration was studied under different FR values and across a range of infusion doses. In addition, the present results extend previous findings (1) by showing that termination of prolonged access to nicotine under conditions in which it functions as a positive reinforcer does not result in physiological dependence.

Ten male hooded rats each implanted with an venous catheter (7) were maintained in standard operant conditioning chambers with food (20-30g/ day) and water always available. Each chamber was enclosed in a sound-attenuating box. Responding on one lever activated an infusion pump for 4-5 seconds, delivering an infusion of 0.13 ml of solution. Responses on the other lever (activity lever) were recorded but had no programmed consequence. The rate of activity lever responding was recorded throughout all experimental manipulations and was compared to the rate of responding recorded from the lever resulting in nicotine infusions. The houselight provided illumination and blinked at a rate of 10 Hz during an infusion. First, nicotine self-administration was established in the rats at 32 µg/kg/infusion (all doses are expressed as the free base). Access to nicotine was unlimited (24 hours), with one response required for each infusion (FR 1). Then changes were made in the nicotine delivery procedure to determine if lever pressing was being maintained by the contingency established between lever pressing and nicotine delivery (4). Changes included substitution of saline for nicotine, systematic changes in dose and programmed nicotine infusions at intervals of 30, 45, 60 and 90 minutes. All rats were tested with the saline substitution procedure and three rats were given programmed infusions. In the seven rats not receiving programmed infusions the effect of infusion dose was determined on the number of infusions delivered and the total nicotine intake (mg/kg/24 hour) under an FR 1 schedule. Infusion doses (64.0, 32.0, 16.0, and 8.0 µg/kg/ infusion) were presented in descending order for a minimum of 7 days each. Under each infusion dose lever pressing was allowed to stabilize before changes were made. In the three rats that received programmed infusions the effects of FR size (1-8 responses/32 µg/kg/infusion) on the number of lever presses and the number of infusions were studied. Ratios were presented in ascending

order and the rats were maintained under each ratio for a minimum of 7-10 sessions.

All rats initiated and maintained nicotine self-administration (Figure 1, left panel). Generally, 10-20 sessions were necessary for the acquisition and stabilization of responding on the nicotine lever. Stability was defined as 3-5 sessions with no increasing or decreasing trends in the number of infusions. The within session pattern of nicotine-reinforced responding under the FR 1 schedule was typically a series of closely spaced infusions (2-4/minute), followed by a pause (30-90 minutes) during which time no infusions were taken. Nicotine self-administration was shown to be maintained by the response-nicotine contingency, rather than by other behavioral effects of nicotine. Substitution of saline for nicotine solution failed to maintain lever pressing (Figure 1). Saline substitution produced a temporary (3-6 hours) increase in lever pressing which rapidly declined to less than 12 infusions during the following 24 hour session. When nicotine was reintroduced (31.0 µg/kg/infusion) the number of nicotine infusions increased to previous levels (Figure 1). Periodic observation of the rats when nicotine was available and during the saline substitution failed to reveal any signs of physical dependence (8). When nicotine was available lever pressing occurred almost entirely on the lever delivering nicotine infusions. Activity-lever responses were less than 10% of the total number of responses for all rats.

Table I shows the effect of programmed infusions delivered independently of responding on nicotine maintained lever pressing. The percent decrease in the number of response contingent infusions was inversely related to the programmed interinfusion interval. The sum of response contingent infusions plus response independent programmed infusions was stable across sessions (Table 1), suggesting that the daily level of nicotine self-administration is at least in part under control of some circulating blood level.

The effect of varying [illegible] dose on the number of infusions under an FR1 schedule is shown in the right panel of Figure 1. As the dose of nicotine was decreased the number of infusions first increased then decreased. In contrast, session intake (mg/kg of body weight) increased as a function of nicotine dose (Figure 1). Similar functional relationships have been found with other reinforcers (4). The 8 µg/kg/infusion dose did not maintain lever pressing above saline levels.

These results demonstrate that intravenously delivered nicotine can increase and maintain lever pressing that results in its delivery. The changes in the nicotine delivery procedure showed that lever pressing was maintained by the nicotine-response contingency. There were four indications of the positive reinforcing effects of nicotine: 1) a greater number of lever presses when nicotine was response-contingent than when saline was response-contingent; 2) a greater number of responses on the nicotine lever than on the activity lever; 3) a systematic decrease in the number of contingent infusions when nicotine was delivered noncontingently; and 4) systematic changes in lever pressing as a function of the nicotine dose.

The effect of increasing the ratio size on the number of lever presses and infusions is shown in Figure 2. Increases in FR size up to FR 5 resulted in substantial increases in the number of lever presses. At ratio of 6 and 7 the number of lever presses remained relatively stable. A further increase in ratio size to FR 8 resulted in a decrease in the number of lever presses. The number of infusions remained relatively stable across several ratios (1-6), then decreased at ratios of 7 and 8. Although intravenously delivered nicotine maintained ratio performance, these overall rates of responding compared to other intravenously delivered reinforcers (4) are low, suggesting that nicotine may be a weak reinforcing agent.

5

Previous attempts to establish nicotine as an intravenously delivered reinforcer for rats have shown that only under conditions of reduced body weight and/or concurrent fixed time food presentation will nicotine self-administration occur at rates above vehicle control levels (3). The present results show that nicotine can function as an intravenously delivered positive reinforcer for rats in the absence of such conditions, and that the level of responding can be maintained across several ratio schedules.

A detailed profile of the behavioral effects of nicotine has been emerging from several laboratories (1,2); however, there has been a continuing need for a systematic evaluation of the reinforcing effect of nicotine in the rat. In this study the maintenance of lever pressing was unequivocally the result of consequent nicotine infusions. Furthermore, the behavior was shown to be sensitive to both dose and response contingency manipulations.

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7. Venous catheters were implanted [J. R. Weeks, in Methods in Psychobiology, R. D. Myers, Ed. (Academic Press London, 1972), 2 pp 134]. Under pentobarbital and ketamine anesthesia and under aseptic conditions. One end of the catheter (inside dimension, 0.3 mm outside dimension, 0.62 mm)

was passed by way of the external jugular vein into the superior vena cava at the level of the right atrium. The distal end of the catheter was passed subcutaneously and out through the skin in the middle of the scapula of the rat's back. The catheter was connected to a stainless steel back plate. Each animal was allowed 10 days recovery before being placed in a test chamber.

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Table 1

The percent decrease in the number of self-administered nicotine infusions and the total number of infusions as a function of the interval between response independent programmed nicotine infusions.

Interinfusion Interval (minutes)	Mean (± standard error) % decrease in the number of self-administered infusions	Mean total infusions (± standard error) programmed plus response contingent
Control		76 (±5.8)
30	59 (± 4.3)	81 (±3.0)
45	45 (± 5.0)	73 (±4.3)
60	30 (± 3.4)	79 (±8.1)
90	21 (± 1.5)	74 (±2.6)

Figure 1. Effects of substituting saline for nicotine on the number of infusions (left panel). Each bar represents a mean of 10 sessions (10 rats x 1, 24 hour sessions). The vertical lines show the standard error. The right side of the figure shows the effect of varying the dose of nicotine on both the number of infusions (solid lines) and session intake (mg/kg/session, dashed lines) under an FR 1 schedule. Each point is a mean of 21 sessions (7 rats x 3 sessions each) and the vertical lines show the standard error.

Figure 2. The number of lever presses and infusions (32 µg/kg) is shown as a function of the FR size. The ratios were presented in an ascending order. Each point is a mean of 9 observations (3 rats x 3 sessions) and the vertical lines show the standard error.

We thank Yvonne Dragan and Lisa Carron for their technical assistance.

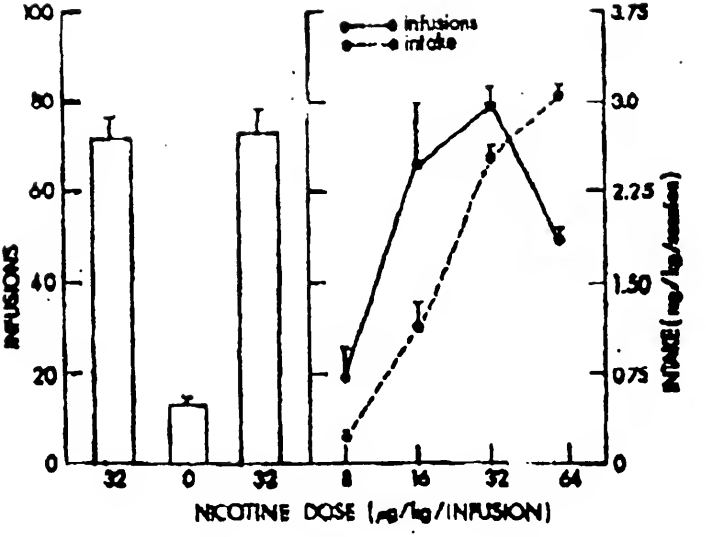
infusions
intake
INFUSIONS
100
80
60
40
20
0
3.75
3.0
2.25
1.50
0.75
0
32
0
32
8
16
32
64
NICOTINE DOSE (μg/kg/INFUSION)

Figure 1

Mr. DENOBLE. This paper was reviewed by my immediate management. I think it was Jim Charles at the time, although it might have been Dr. Dunn. I don't remember exactly when we changed. It was reviewed by them, then sent to the director of research, Dr. Osdene. From there it gets kind of fuzzy, I don't know where it goes. But it comes back about 2 weeks later with a yes or a no.

Mr. WYDEN. Approval was given to submit it to this Psychopharmacology Journal?

Mr. DENOBLE. To Psychopharmacology, as well as to the American Psychological Association meeting in Anaheim, coming up in 1983.

Mr. WYDEN. All right. Let me ask you, if I might, about some later events at Philip Morris. You were promoted in 1983?

Mr. DENOBLE. Yes, I was.

Mr. WYDEN. And your supervisors evaluated your performance and gave you favorable marks over all?

Mr. DENOBLE. Yes. We were given evaluations each year that we were there.

Mr. WYDEN. Did you get raises?

Mr. DENOBLE. Yes, we did, every year that we were there.

Mr. WYDEN. How about your associate, Dr. Mele?

Mr. MELE. Yes, the same thing.

Mr. WYDEN. All right. Now, we're also interested in some developments in mid-1983, where you and some researchers flew from Richmond, Va. to New York City, to brief the senior management on your work. Can you walk us through what happened in some of those key events that started back in Richmond?

Mr. DENOBLE. Sure. We were notified by our senior management that we were going to be going to New York corporate headquarters to give a presentation on the activities of the behavioral pharmacology laboratory. We were taken to the airport, put on a company jet, flown up to New York, and one of the PM-1 limousines met us and took us over to the corporate headquarters.

At that point, we gave a presentation to several members of New York corporate staff, entertained questions, had lunch in corporate executive dining room, and then were flown back that evening on the company jet.

Mr. WYDEN. What kind of questions were you asked at the New York briefing?

Mr. DENOBLE. I was only asked one question.

Mr. WYDEN. What was that?

Mr. DENOBLE. I can't quote it but I'll paraphrase it. It's basically, "Why should I risk a billion dollar industry on rats pressing a lever to get nicotine?"

Mr. WYDEN. And this was a Philip Morris executive that asked you that question?

Mr. DENOBLE. Yes.

Mr. WAXMAN. Could the gentleman yield to me?

Mr. WYDEN. I'd be happy to.

Mr. WAXMAN. Could you tell us who was at this meeting?

Mr. DENOBLE. I've been wracking my brain and I can't. There is only one individual that I can remember who was there and that was a lady named Carolyn Levy, Dr. Levy.

Mr. WAXMAN. Were these top management people?

Mr. DENOBLE. Yes, they were.

Mr. WAXMAN. Thank you, Mr. Wyden.

Mr. WYDEN. Would it be fair to say that the senior management people were troubled or worried about the work that you were doing?

Mr. DENOBLE. From that meeting, I didn't think so. In fact, on the way back in the plane, we all thought things went very, very well. However, subsequently after that meeting, we were told that our laboratory might be shut down, but they wanted to continue the research. And the possibility was that we would set up a laboratory in Lusanne, Switzerland, to continue the research.

Mr. WYDEN. Let me ask you specifically about a matter a couple of weeks after the meeting. Were you told a couple of weeks after the meeting, by several of the Philip Morris management, that your lab was generating information that the company did not want generated inside the company?

Mr. DENOBLE. That is correct. Apparently, at the time some litigation had come out, some lawsuits. And we were told that the data we were generating, and the types of studies that we doing, would not be favorable in that litigation.

Mr. WYDEN. Were you told then that the top management was looking at a couple of specific options, one of them was releasing you and your associate from employment, and possibly trying to look at some other arrangement?

Mr. DENOBLE. Yes. Two options were discussed. One was to release us from employment but employ us as contract individuals somewhere in Richmond or somewhere close to the research center, because the scientists at Philip Morris down in Richmond, felt the research should continue.

Then there was the idea, the discussion that really doesn't remove it from the company as much as they would like it, so they talked about sending us to Lusanne, Switzerland, at a contract facility.

Mr. WAXMAN. Could the gentleman yield?

Mr. WYDEN. I'd be happy to yield, Mr. Chairman.

Mr. WAXMAN. Could we get for the record, who was telling you these things?

Mr. DENOBLE. Dr. Jim Charles and Dr. Tom Osdene.

Mr. WAXMAN. They were with you at Philip Morris in Richmond?

Mr. DENOBLE. Yes. Dr. Charles was our immediate supervisor. He was the manager of the biochemistry group. Dr. Osdene was the research director and reported to the vice president.

Mr. WAXMAN. And both of those options were to have you do the work, but not in house?

Mr. DENOBLE. That is correct.

Mr. WAXMAN. Did they give you a reason?

Mr. DENOBLE. They just said that if the work were removed from the company, connecting it back to the company would be, you know, more difficult to do than if it's being done right in the company itself.

Mr. WAXMAN. That's what we call deniability.

Mr. DENOBLE. I'm sorry, sir, I don't know.

Mr. WAXMAN. Mr. Wyden?

Mr. WYDEN. Dr. Mele, can you confirm that these discussions took place?

Mr. MELE. Yes, they did.

Mr. WYDEN. All right. Let's turn, if we could now, to August of 1983. The company was involved in the Cipollone case, sued. One of the claims, of course, was that cigarettes were dangerous because they were addictive.

Now, to begin with, the self-administration paper that you submitted to pharmacology, I understand that in August of 1983, about the time of the lawsuit, this paper was accepted for publication, but at essentially that time you were told that you could not publish it?

Mr. DENOBLE. That is correct. I was told to withdraw it.

Mr. WYDEN. And let us now make sure we understand the status of that paper because, you know, to me this is one of the kinds of key concerns I have, because right at a time when the company has some exposure, and there is independent science generated within the company, the company is still trying to push it aside; and I'm curious about the status of the paper. At that time, had the paper gone through peer review at this particular journal?

Mr. DENOBLE. Yes. It had been reviewed by Dr. Barry and two anonymous reviewers.

Mr. WYDEN. So it had been officially accepted for publication?

Mr. DENOBLE. Yes.

Mr. WYDEN. And were you told by management that you would have to withdraw it?

Mr. DENOBLE. Yes, I was.

Mr. WYDEN. Did management say that it could help plaintiffs in litigation, if it was published?

Mr. DENOBLE. I don't believe they said that. But they did say that if it—actually they said, if it were published, it wouldn't be good for litigation.

Mr. WYDEN. And you protested at that time?

Mr. DENOBLE. Oh, yeah, we both did, very much so.

Mr. WYDEN. You said that, in effect, you were a scientist and you had an obligation to let science go forward unfettered, and it would be embarrassing to retract the paper after acceptance?

Mr. DENOBLE. I would love to say I said it that way, but I basically protested——

Mr. WYDEN. Don't let me characterize it. You say it.

Mr. DENOBLE. I basically protested and felt that the paper was released. It had been approved, it should have been published, that there was no doubt about that. We protested both to our immediate manager, Jim Charles and also to the director of research, Dr. Osdene.

Mr. WYDEN. And you wrote in August of 1983 to the Journal withdrawing publication? You said you were withdrawing the manuscript due to factors beyond your control?

Mr. DENOBLE. That is correct.

Mr. WYDEN. All right. Mr. Chairman, I would like that letter introduced into the record as Exhibit 12, and note that my time has expired.

Mr. WAXMAN. Without objection, it will be in the record as Exhibit 12.

[Exhibit 12 follows:]

PHILIP MORRIS RESEARCH CENTER,
P.O. Box 26583, Richmond, VA, August 30, 1983.

Herbert Barry, III, Ph.D.,
University of Pittsburgh,
School of Pharmacy, Pittsburgh, PA

DEAR DR. BARRY: I regret to inform you that due to factors beyond my control I must withdraw our manuscript #8381400 from consideration as a publication in *Psychopharmacology.*

Please accept my sincerest apology.

Sincerely,

VICTOR J. DENOBLE, PH.D., ASSOCIATE SENIOR SCIENTIST.

Mr. WAXMAN. Does the gentleman want additional time?

Mr. WYDEN. Yes, if that would be acceptable. Maybe a couple of more questions at this point would be helpful, Mr. Chairman.

Now, Dr. DeNoble, you were scheduled to go to California to present your work before the American Psychological Association. This was supposed to be a process, a program of a poster presentation. What is that, and what happened to your presentation?

Mr. DENOBLE. Well, a poster presentation is very much like the posters you have over here. You would take an introduction of what the experiment was, a title, and you put all your results up, and you put your conclusions up. It's basically a 3-hour poster session in which you stand by the presentation for at least an hour, a minimum of an hour, and discuss your research with other scientists who are at the meeting.

Mr. WYDEN. Were you told by the top management at Philip Morris that you couldn't make a poster presentation?

Mr. DENOBLE. Yes, we were. I was.

Mr. WYDEN. And did they tell you why you couldn't make a poster presentation?

Mr. DENOBLE. It had to do with the effects that—facts that this would not look good in the current litigation.

Mr. WYDEN. OK. At that time, did you get a visit from a small battalion of lawyers at Philip Morris, over at your lab?

Mr. DENOBLE. Well, a couple of them came, yes. We did get visited by several attorneys.

Mr. WYDEN. Three or four, or how many?

Mr. DENOBLE. Give me a second, please.

[The witness confers with Mr. Mele.]

Mr. DENOBLE. There were at least three attorneys.

Mr. WYDEN. OK. And they basically set up shop next to your lab and brought their xerox machine and started rummaging around your documents and files?

Mr. DENOBLE. They did go through my files; they went through Paul's files as well. They took documents and placed them in red folders. These red folders were then documents that they would photocopy. They did not remove anything from the lab, they just photocopied everything they thought was important.

Mr. WAXMAN. Will the gentleman yield to me?

For the record, do you recall the names of any of those attorneys?

Mr. DENOBLE. Yes. There was Fred Newman. I believe he was a corporate attorney from New York. Rhonda Fawcett, who was from an agency called Shook, Hardy, and Bacon, in Kansas City; and her two supervisors, and I do not remember their names.

Mr. WAXMAN. She was from a law firm?
Mr. DENOBLE. She was from a law firm in Kansas City.
Mr. WAXMAN. And two of her supervisors from the law firm?
Mr. DENOBLE. Yes.
Mr. WAXMAN. OK.
Mr. WYDEN. Let me, if I could possibly understate this, Dr. DeNoble. Isn't it a little bit unusual to have a paper like this, after it has been peer reviewed, accepted for a journal, suppressed, a poster presentation canceled, and then to have a visit by three or four lawyers, isn't that a little bit unusual?
Mr. DENOBLE. Yes, sir, it is.
Mr. WYDEN. OK. Mr. Chairman, thank you.
Mr. WAXMAN. Thank you, Mr. Wyden. I'm going to recognize myself for another round of questions. Let me just see if I understand the chronology here. You went to work in 1980. You were doing work in 1980, 1982. By June of 1983 you went to New York and you met with some of the top executives at Philip Morris. You are telling them what you were doing in your lab work, that was June 1983.
In August, you wanted to publish your paper. You were told when you were hired that you could publish papers. And now you were being told you couldn't publish this paper or make a presentation to the American Psychological Association.
That August 1983 is a significant time as well, because on August 1, 1983, the Cipollone case was filed. The Cipollone was a case of going against Philip Morris for liability for a death resulting from cigarette smoking.
Now, as Mr. Wyden indicated, you started to get more concern expressed by people at Philip Morris. People were suggesting, your supervisors were suggesting, perhaps you ought to go outside of Philip Morris and do your work, go to Switzerland to an independent lab from where you were.
And you next had visits from these lawyers that came by, and they were looking very carefully at your work. I'd like to jump ahead 2 months to November of 1983. Your laboratory had a visit from Shep Pollack.
According to Moody's Industrial Manual from 1983, Shep Pollack was an important person at Philip Morris. In fact, he was the president and chief operating officer of Philip Morris, U.S.A. He was also on the Board of Directors of the parent company, Philip Morris, Incorporated.
Who visited the laboratory with Mr. Pollack?
Mr. DENOBLE. He was accompanied by Mr. Fred Newman, the attorney I mentioned previously.
Mr. WAXMAN. And——
Mr. DENOBLE. And also by, I'm sorry, also by Jim Charles, I believe, or Dr. Osdene. But they didn't tour the lab, just Mr. Newman and Mr. Pollack.
Mr. WAXMAN. And what happened at that meeting?
Mr. DENOBLE. We toured the laboratory facility. We set up a demonstration for Mr. Pollack, that he could actually see the animals working for food, or/and pressing the lever for nicotine.
Mr. WAXMAN. You had a demonstration of the rat actually self-administering?

Mr. DENOBLE. Yes. It was easy to do. The lab was situated such that if we stood in the operating room, we could see the self-administration room, and those doors could be left open. And we could also sit and look into the experimental room where the animals would work for food, and those doors—we had to train animals to actually work——

Mr. WAXMAN. Just so we can understand this. I think we have a photograph of what that cage looked like. That was Exhibit 8, earlier referred to but not shown to the committee.

So what happened?

Mr. DENOBLE. That's a single experimental chamber in our self-administration room. As I indicated, there is a little lever or switch, and you can see levers in the boxes. The animal has access to water and food. There is a pump on top of the box, and there is a solution behind it, probably of either nicotine or acetaldehyde. The animal is hooked up to the tether that hangs down in the box, and can press the lever to deliver the solution into its vein.

Mr. WAXMAN. So you are there with the president of Philip Morris, showing him how these rats self-administer nicotine in their brain——

Mr. DENOBLE. In their heart.

Mr. WAXMAN. This was in their heart?

Mr. DENOBLE. Yes.

Mr. WAXMAN. And that this is a reinforcing agent? I assume that you went through all of that information for——

Mr. DENOBLE. Yes. The interesting thing was, I mean, the question brought out of course, was, you know, was this addiction? And——

Mr. WAXMAN. Who asked that question?

Mr. DENOBLE. Mr. Pollack. And I went into my routine. It's not addiction, it's a reinforcing agent and it predicts abuse liability. So it was an opportunity to do some educating.

Mr. WAXMAN. What did Mr. Pollack say about that?

Mr. DENOBLE. He accepted the answer. We chatted about that and we moved forward.

Mr. WAXMAN. What about Fred Newman, he was the lawyer, did he ask any questions?

Mr. DENOBLE. Mr. Newman asked if this test procedure was the same test procedure that a government agency would use to demonstrate addiction? After I corrected him about addiction, I did say it's the exact procedure that NIDA would use to demonstrate abuse liability, yes.

Mr. WAXMAN. And NIDA is?

Mr. DENOBLE. The National Institute of Drug Abuse.

Mr. WAXMAN. OK. And what was his reaction to that?

Mr. DENOBLE. He was not very happy with that reaction. He basically shook his head and walked off.

Mr. WAXMAN. Dr. Mele, can you confirm this report of this meeting with Shep Pollack, the president of Philip Morris in visiting the lab in November of 1983?

Mr. MELE. Yes. He did visit, he toured the lab, and he did ask the question, and it was responded to just as Dr. DeNoble says.

Mr. WAXMAN. Let me make an observation about the significance of what you are telling us, because to this day Philip Morris has

maintained that nicotine is not addictive, and it is in cigarettes only for its taste.

Yet it is now clear that 10 years ago, the president of Philip Morris, the president of the company, visited your lab and actually witnessed a rat injecting himself with nicotine. This rat was not doing that because of the taste of nicotine, and the rat wasn't pressing the lever to get more nicotine because of peer review.

The rat was pressing this lever in order to self- administer nicotine because this was something that rat physiologically wanted. And he was told by you that nicotine is a reinforcing drug that has an abuse liability? Is that a correct statement?

Mr. DENOBLE. [Nodding affirmatively.]

Mr. WAXMAN. What was the immediate result of the visit by Shep Pollack? Were you told to continue your research?

Mr. DENOBLE. Actually, yes. Two weeks later we were given a green light to just go ahead. We actually hired another person in, a contract person. We were told that everything was fine and to just run full force, and we did. So we just kept doing experiments.

Mr. WAXMAN. This was the end of the year beginning in 1984. And in April of 1984, Philip Morris made a decision to close down the laboratory. Could you please recount for us the closing of the lab?

Mr. DENOBLE. I believe it was the second Thursday. It was April 5th, the first Thursday, in 1984. It was at 3 in the afternoon, and Dr. Charles, Jim, called me to his office and was telling me what a great job we had done for the company.

Quite frankly, I thought this was great and we were getting a lot of accolades. I was getting a lot of accolades, and Paul. And he said, "However, we are discontinuing animal research beginning now."

I was told that Paul had to come up and talk to him. And I was basically to shut the equipment off; terminate the experiments, even if they were ongoing; to kill all the animals the following day; and that was the end. We were—our badges were discontinued access to the research center. By the following Monday, we couldn't get back in.

We were provided offices, we were provided secretarial support, we were provided funds to look for other jobs. Quite frankly, the company was very gracious to us during that time, but the lab was literally shut down.

Mr. WAXMAN. When you were told they were shutting down your lab, what was your reaction? What did you say to them?

Mr. DENOBLE. Why? I mean, you know, why? All of a sudden everything was going down the tubes, and the response that I immediately got was that it was a business decision. I mean, that's the only thing they said to us during the first couple of weeks it was shut down.

Mr. WAXMAN. Did you ask for, at least for a short period of time, to complete some of the work that was ongoing?

Mr. DENOBLE. To do anything. I mean, just to complete manuscripts, and we were not able to do that. We weren't able to continue.

Mr. WAXMAN. Is it accurate that you asked for at least another day to get some more data?

Mr. DENOBLE. We did. We were able to get that Friday to. Right, we went back the next day on Friday and we did kill all our rats. And at that point, the lab was over, it was ended.

Mr. MELE. May I add something here?

Mr. WAXMAN. Yes. Dr. Mele.

Mr. MELE. Because I was going through this recently, we did—that Friday was a critical day to end one study. I don't remember what the study was, but it was a final manipulation of a long series of manipulations. And we did ask for permission to, at least, finish that study. And that was denied.

Mr. WAXMAN. What do you mean, manipulations?

Mr. MELE. It was a chronic dosing study, and this was the day where the animals would have been tested to see how they responded. I don't remember, again, the details of the study, but we did try and get that one final data point, and they didn't even want us to continue that much. It wasn't of much interest to the company, it was of interest to us.

Mr. WAXMAN. Did you ever go back to the lab?

Mr. DENOBLE. I had the occasion to go back to the lab a few days later, the following week, because I had the combination to a safe where we kept some controlled substances, yes.

Mr. WAXMAN. And what did you find?

Mr. DENOBLE. The lab was gone, everything was gone. The equipment was gone, the cages were gone, the animals were gone, all the data was gone. It was empty rooms.

Mr. WAXMAN. Was it as if there had never been a lab there before?

Mr. DENOBLE. You'd probably think there was, but there was no evidence there was any behavioral lab there. The only thing that was there was the safe. Everything was gone. It was just gone.

Mr. WAXMAN. OK. Thank you. Mr. Bliley?

Mr. BLILEY. Dr. DeNoble, could you clarify one point for me? Earlier you mentioned lawyers from Philip Morris being in your lab in 1983. Isn't it correct that they were in your lab to collect documents to be produced in a lawsuit, perhaps the Cipollone case?

Mr. DENOBLE. I believe that is correct, yes.

Mr. BLILEY. And, Mr. Chairman, could we keep the record open so that we can submit some questions in writing to these two gentlemen?

Mr. WAXMAN. Without objection, we will keep the record open, and members of the subcommittee may have additional questions they'll want you to respond to in writing. For the record, we would ask you to make those responses.

Mr. BLILEY. Thank you, Mr. Chairman, I have no further questions.

Mr. WAXMAN. Thank you, Mr. Bliley. Mr. Synar?

Mr. SYNAR. Thank you, Mr. Chairman. Doctor, let me move on to this issue of your termination of employment.

After the lab closed, what career options did Philip Morris give you?

Mr. DENOBLE. There were three options that were offered to us. One was to stay with the company, the second one was to receive a cash pay-out, and the third was to continue us on the payroll until we located new positions elsewhere.

Mr. SYNAR. What option did you take?

Mr. DENOBLE. Well, originally we took the option of staying with the company. We figured times were tough in the 1980's, and jobs were very difficult to come by, so we said, we'll stay with the company. And we were then informed that if we did do that, that significant reductions in salary, as well as positions—there was even discussions of, well, you may in fact have to go sweep the floor somewhere, if we stayed with the company.

So it was clear that they didn't want us to be there. So the second option we both elected was to continue on salary until we located new positions.

Mr. SYNAR. So, ultimately, what happened?

Mr. DENOBLE. Ultimately, we both found new jobs.

Mr. SYNAR. OK. When you left Philip Morris, were you free to talk about your work, or were you covered by a secrecy agreement?

Mr. DENOBLE. I think we were—we were still covered by that agreement, so we kept it pretty low profile at the time. At least we thought it was low profile. We were pretty upset about this, so we didn't talk about it very freely.

Mr. SYNAR. Let's move this story on beyond that. It didn't end after you left Philip Morris. In 1985 and 1986, you both made various efforts to publish and present some of your work. And I'm told, for instance, and we have a letter and an article to this effect, you sent the Journal in December of 1985. That letter, I think, is Exhibit 13. I'd ask unanimous consent that it be made part of the record.

Mr. WAXMAN. Without objection, that will be——

Mr. SYNAR. And the article is Exhibit Number 14.

Mr. WAXMAN. And the same for that.

[Testimony resumes on p. 92.]

[Exhibits 13 and 14 follow:]

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December 31, 1985

JAN 8 1986

Herbert Barry, III, Ph.D.
University of Pittsburgh
School of Pharmacy
Pittsburgh, Pennsylvania

Dear Dr. Barry:

Enclosed you will find a manuscript entitled "Intravenous Nicotine Self-Administration in Rats: Effects of Mecamylamine, Hexamethonium and Naloxone", which we would like reviewed for publication in Psychopharmacology.

Since this paper is an extension of a previously reviewed manuscript (MS-83 B-1400), which was withdrawn, I have enclosed copies of the original communications. I trust the manuscript is in order, and look forward to your response.

Sincerely,

Victor J. DeNoble, Ph.D.
CNS Pharmacology

VJD:tbk
encl

INTRAVENOUS NICOTINE SELF-ADMINISTRATION IN RATS: EFFECTS OF MECAMYLAMINE, HEXAMETHONIUM AND NALOXONE*

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ABSTRACT

Victor J. DeNoble and Paul C. Mele, Intravenous Nicotine Self-Administration in Rats: Effects of Mecamylamine, Hexamethonium and Naloxone. Psychopharmacology 000,000.

The rate and pattern of lever pressing were studied in eighteen rats during 24 h sessions in which responding resulted in intravenous (iv) infusions of nicotine. There were four indications of the positive reinforcing effect of nicotine: 1) a greater number of lever presses when nicotine was response-contingent compared to when saline was available; 2) a greater number of responses on the lever resulting in an infusion of nicotine than on the control lever; 3) systematic decreases in the number of contingent nicotine infusions when nicotine was delivered noncontingently; 4) systematic changes in the frequency of lever pressing as a function of dose. Under a fixed-ratio 1 (FR 1) schedule the number of infusions first increased and then decreased as the dose of nicotine was decreased (64, 32, 16, 8 µg/kg infusion) and nicotine intake (mg/kg/24 h) was directly related to the infusion dose. As the FR size was increased from 1 to 6, the number of lever presses increased and the number of infusions (32 µg/kg) remained stable. At FR values greater than six, both the number of lever presses and infusions decreased. Presession injections of mecamylamine (0.75, 1.5 and 3.0 mg/kg sc) decreased the number of infusions in a dose related manner. Presession injections of hexamethonium (1.5 and 3.0 mg/kg sc) or

naloxone (0.75, 1.5 and 3.0 mg/kg sc) did not alter the within or between session patterns of nicotine selfadministration. Under the conditions of the present experiment nicotine served as an effective reinforcer and the behavior was shown to be sensitive to both FR size and infusion dose. In addition, the results suggest that nicotine self-administration involves central nicotinic receptors and that opioid receptor antagonism has no effect on nicotine's reinforcing effects in rats.

Key Words: Nicotine self-administration, FR schedules, noncontingent nicotine infusions, mecamylamine, hexamethonium, naloxone, rats.

The effects of nicotine on schedule-controlled behavior have only recently been systematically studied (Morrison and Stephenson 1969; Pradhan 1970; Ando 1975; Davis et al. 1973; Spealman et al. 1981; DeNoble et al. 1982 a,b). In rats, nicotine increases responding maintained by fixed-interval (FI), variable-interval and differential reinforcement of low rate schedules of food or water presentation and by schedules of electric shock postponement (Bovet and Bovet-Nitti 1965; Morrison 1967; Pradhan 1970; Ando 1975). In contrast, nicotine decreases responding maintained by FR schedules of food or water presentation (Morrison 1967; Pradhan 1970). Qualitatively similar results have been reported in squirrel monkeys maintained by a multiple FI-FR schedule of either presentation of food or termination of a stimulus associated with electric shock (Davis et al. 1973; Spealman et al. 1981).

Many drugs from different pharmacological classes can increase and maintain behavior that leads to self-administration of those drugs (Pickens et al., 1978). It has been shown that iv injections of nicotine will maintain high rates of lever pressing by squirrel monkeys under a second-order or FI schedule (Goldberg et al. 1981; Spealman and Goldberg 1982). Under the second-order schedule, responding results in the presentation of a visual stimulus that is intermittently associated with response-contingent nicotine injections. However, there is little evidence that rats will self-administer nicotine intravenously unless self-administration is induced by a concurrent food delivery schedule (Lang et al. 1977; Smith and Lang, 1980). Even when rats are given pro-

grammed nicotine infusions for several days (Hanson et al. 1979) the levels of responding maintained by iv nicotine following the programmed infusions have been reported to be low. The present study demonstrates that iv delivered nicotine functions as a positive reinforcer in rats in the absence of food inducement or programmed infusion conditions. Nicotine self-administration was studied under different FR values and across a range of infusion doses. In addition, the effects of mecamylamine, hexamethonium and naloxone on nicotine maintained lever pressing were evaluated.

METHODS

Subjects. Eighteen experimentally naive male Long Evans hooded rats (Blue Spruce Farms) weighing 350 to 400 g were used. Pats were anesthetized with ketamine (70 mg/kg/im) and sodium pentobarbital (18 mg/kg/ip) and implanted with a venous catheter under aseptic conditions. One end of the catheter (inside diameter, 0.30 mm; outside diameter 0.61 mm) was passed by way of the external jugular vein into the superior vena cava at the level of the right atrium. The distal end of the catheter was passed subcutaneously and out through the skin in the middle of the rat's back. This end of the catheter was connected to a stainless steel back plate and via protective tubing and swivel joints it was connected to a remote infusion pump. Each rat was allowed seven days recovery in its home cage before being placed in the test chamber. The general catheterization procedure has been described in detail elsewhere (Weeks 1972).

Apparatus. Nine identical operant conditioning chambers (Lehigh Valley Electronics, LVE No. 193-25), each contained in a sound-attenuated cubicle (LVE No. 132-02) were used. Located at one end of the chamber were two levers, six cue lights (lever lights), a house light and water spout. Presses on the right lever were programmed to activate the infusion pump (Harvard Apparatus Peristaltic Pump No. 1201) for 4s, delivering an infusion of 137 µl of solution into the blood stream of the rat. The pattern of responses was recorded on strip chart recorders. Responses on the left lever (control lever) were recorded but had no programmed consequences. The house light (4.5 watts) provided general illumination and blinked at a rate of 10 Hz when the infusion pump was activated. White noise was continuously present and an exhaust fan provided ventilation. During all experimental sessions (20-30 g) Purina Rat Chow and unlimited water were available. Experimental events were scheduled and responses recorded by equipment located in an adjacent room.

Lever pressing maintained by nicotine infusions. Responding by 10 rats was established and maintained by an FR 1 schedule of iv nicotine infusions (32 µg/kg). Experimental sessions lasted 24 h. After responding developed and stabilized (3-5 days with no increasing or decreasing trends in the number of nicotine infusions per day) changes were made in the nicotine delivery procedure to determine if lever pressing was being maintained by the contingency established between lever pressing and nicotine delivery (Pickens et al. 1978). Changes included substitu-

tion of saline for nicotine, systematic changes in dose, and, the addition of programmed response independent nicotine infusions at intervals of 30, 45, 60 and 90 min. The rate of control lever responding was recorded throughout experimental manipulations and was compared to the rate of responding recorded from the lever resulting in nicotine infusions. All rats were tested with the saline substitution procedure and 3 rats were given programmed infusions. In the 7 rats not receiving programmed infusions the effect of infusion dose was determined on the number of infusions delivered and the total nicotine intake (mg/kg/24 h) under an FR 1 schedule. Infusion doses (64, 32, 16 and 8 µg/kg/infusion) were presented in descending order for a minimum of 7 days each. At each infusion dose, lever pressing was allowed to stabilize before changes were made. In the 3 rats that had received programmed infusions the effects of FR size (1-8 responses/32 µg/kg/infusion) on the number of lever presses and the number of infusions were studied. Fixed-ratios were presented in ascending order and the rats were maintained under each ratio for a minimum of 7 to 10 sessions.

Effects of mecamylamine, hexamethonium and naloxone on nicotine-maintained responding under a FR 1 Schedule. Responding by 8 other rats was established and maintained under a FR 1 schedule of iv nicotine infusions (32 µg/kg) in experimental sessions that lasted 24 h. After responding developed and stabilized (3-5 days with no increasing or decreasing trends in the number of nicotine infusions) saline was substituted for nicotine.

After saline substitution the rats were restabilized under the FR 1 schedule of iv nicotine infusion (32 ug/kg per infusion) and 4 rats were given presession injections of saline followed 24 h later by a presession injection of mecamylamine (0.75, 1.5, 3.0 mg/kg/sc). These same 4 rats were also treated at a later time with hexamethonium (1.5 and 3.0 mg/kg/sc). The doses of mecamylamine used in this study were chosen on the basis of previous findings that 1.0 - 3.0 mg/kg of mecamylamine can block the behavioral effect of nicotine (Schecter and Rosecrans 1972; DeNoble et al. 1982a; Spealman and Goldberg 1982) without altering baseline responding. The hexamethonium doses were chosen on the basis that it does not readily peretrate the central nervous system but is effective at blocking the peripheral effects of nicotine (McIssac 1962). The remaining four rats were given presession saline injections followed 24 h later by presession injections of naloxone (0.75, 1.5, 3.0 mg/kg/ip). These doses of naloxone were chosen since doses below 1.0 mg/kg are mu receptor antagonist whereas above 1.0 mg/kg naloxone antagonizes other opioid receptors (Romer et al. 1981; Leander et al. 1982). All injections were given in descending order and separated by 5 days.

Drugs. Nicotine hydrogen (+)-tartrate (Chemical Procurement Laboratories, NY), mecamylamine HCl, hexamethonium and naloxone were dissolved in 0.9% saline solution. Solutions were diluted so that all presession injections were of equal volumes of 1 ml/kg. Nicotine infusion dose is expressed as the free base and presession antagonist injections as the salt.

RESULTS

Acquisition and Maintenance of Responding Under the FR 1 Schedule of Nicotine Infusion. Responding under the FR 1 schedule was initiated and maintained by 32 µg/kg infusions of nicotine in all rats (72 infusion per 24 h session ± 6 SEM). The number of infusions stabilized in all rats within 24 days. The average ± SEM number of days for acquisition of stable behavior to be acquired was 18 days (± 2). The range

INSERT FIG. 1

and the general pattern of acquisition is shown in Fig. 1 for the rat with the shortest acquisition time (dashed lines) and the rat with the longest acquisition time (solid lines). Most rats maintained acquisition patterns similar to those shown in Fig. 1 with the major characteristic being 2 to 5 days of low responding (4 to 30 infusion/24 h) followed by a gradual (3 to 5 days) increase to near stable response rates. The within session pattern of nicotine infusions under the FR 1 schedule was typically a series of closely spaced infusions (2 to 4 per min), followed by a pause (30 to 90 min) during which time little or no infusions were taken.

Effect of Saline Substitution, Nicotine Dose and Programmed Nicotine Infusions on Nicotine Maintained Responding. Substitution of saline for nicotine solution failed to maintain lever pressing. Saline substitution produced a temporary (4 to 8 h) increase in lever pressing, which rapidly declined to less than 12 infusions (± 2 SEM) during the following 24 h session. Periodic observation of the rats when nicotine was available and during the saline substitution failed to reveal any signs of physical dependence (anorexia, pilo-erection, impaired motor activity or convulsions). When nicotine was reintroduced (32 µg/kg) the number of infusions increased to previous levels within 48 h (74 ± 6 SEM). The average ± SEM daily nicotine intake during this condition was 2.5 ± 0.08 mg/kg. When nicotine was available lever pressing occurred almost entirely on the lever delivering nicotine infusions and control lever responses were less than 10% of the total number of responses for all rats.

INSERT FIG. 2

The effect of varying nicotine dose on the number of infusions under a FR 1 schedule is shown in the left panel of Fig. 2. As the dose of nicotine was decreased the number of infusions first increased, then decreased. In contrast, session intake (mg/kg of body weight) increased directly as a function of nicotine dose (Fig. 2 right panel). The 8 µg/kg/infusion dose maintained lever pressing just above saline levels. A retest of the 32 µg/kg dose was not different from the original values ($\bar{x}$ ± SEM = 74 ± 3 infusions/24 h).

INSERT FIG. 3

Figure 3 shows the effect of programmed infusions delivered independently of responding on nicotine-maintained lever pressing. The percent decrease in the number of response-contingent infusions was inversely related to the programmed interinfusion interval (solid line). The sum of response contingent infusions plus response independent programmed infusions was stable across sessions (dashed line).

Effect of Varying FR Size on Nicotine Maintained Lever Pressing. The effect of increasing the FR size or the number of lever presses and infusions (32 µg/kg) is shown in Fig. 4. Increases in ratio size up to

INSERT FIG. 4

5 resulted in substantial increases in the number of lever presses (Fig. 4). At ratios of 6 and 7 the number of lever presses remained stable and a further increase in ratio size to 8 resulted in a decrease in the number of lever presses. The number of infusions also remained stable across several ratios (1 to 6), then decreased at ratios of 7 and 8 (dashed line Fig. 4).

Effects of Mecamylamine, Hexamethonium or Naloxone on Nicotine Maintained Responding. Before each mecamylamine administration responding by four rats was examined in sessions in which a subcutaneous saline injection was given (Fig. 5, open bar). When mecamylamine (0.75

INSERT FIG. 5

mg/kg/sc) was administered there was no change in the total (24) number of infusions. In contrast, mecamylamine at a dose of 1.5 mg/kg decreased the number of infusions by 62%. Increasing the dose of mecamylamine to 3.0 mg/kg decreased responding for nicotine further (Fig. 5, solid bars). Responding for nicotine returned to previous levels the 24 h session after the mecamylamine administrations. Presession treatment with hexamethonium (1.5 and 3.0 mg/kg/sc) in the same four rats did not reduce responding (Fig. 5, bars with dashed lines).

INSERT FIG. 6

The within session pattern of responding following saline and mecamylamine treatment are shown in Fig. 6. The solid line, closed circle function shows the pattern of infusions for 24 h periods in 3 h blocks beginning at 0830 h. This pattern was characteristic for all four animals and the largest standard error for any 3 h period was 2.1 infusions/3 h block. The number of infusions during the first 3 h following the 0.75 mecamylamine dose was elevated compared to saline levels. This was followed by a decrease in infusions in the next 3 h. The number of infusions gradually increased to control values. The number of infusions following the 1.5 mg/kg dose of mecamylamine initially increased (first 3 h) then decreased to near zero levels for 6 of the remaining 3 h intervals. During the last 3 h interval the number of infusions increased by was still below control levels. The 3.0 mg/kg dose decreased the number of infusions in all 3 h intervals. The number and pattern of infusions during the next 24 h period did not differ

from control values. In contrast, injections of hexamethonium (Fig. 5) or naloxone did not alter the total number of infusions 5) or change the within session pattern.

DISCUSSION

Lever pressing by rats was initiated and maintained under an FR schedule by iv infusions of nicotine. These results demonstrate that iv delivered nicotine can increase and maintain lever pressing that results in its delivery. The changes in the nicotine delivery procedure showed that lever pressing was maintained by the nicotine contingency. There were four indications of the positive reinforcing effects of nicotine: 1) a greater number of lever presses when nicotine was response-contingent than when saline was response-contingent; 2) a greater number of responses on the nicotine lever than on the control lever; 3) a systematic decrease in the number of contingent infusions when nicotine was delivered noncontingently; 4) systematic changes in lever pressing as a function of the nicotine dose.

Several previous reports have examined the maintenance of responding by iv infusions of nicotine under an FR 1 schedule in rats (Clarke 1969; Lang et al. 1979; Singer et al. 1978; Hansen et al. 1979; Latiff et al. 1980). Although self-administration of nicotine was demonstrated in most of these studies the rates of responding were generally lower than those maintained by other reinforcers under similar conditions (Pickens et al. 1978). In addition, several previous studies

...y under conditions of reduced body weight and/or concurrent fixed-time food presentations will nicotine maintain rates of responding above those maintained by saline (Lang et al. 1977; Latiff et al. 1980). In the present study, however, several doses of nicotine maintained lever pressing above saline levels in the absence of weight reduction procedures or fixed-time food presentations. One possible explanation for the different effects of nicotine in the present study is that nicotine's reinforcing effects were not associated with delivery of another reinforcer (food). Under conditions of fixed-time food delivery, self-administration of nicotine may be controlled only in part by the pharmacological consequences of nicotine and the inducing schedule may be required to maintain the self-administration behavior (Falk and Samson 1975).

In most previous studies with rats only one response was required to produce a nicotine infusion (Clark 1969; Lang et al. 1977; Hanson et al. 1979; Latiff et al. 1980). However, in the present study when the ratio size was increased the number of lever presses increased across several ratios such that a relatively stable level of daily infusions was obtained. Although in the present study iv delivered nicotine maintained ratio performance, the overall rates of responding under the various ratio sizes were low compared to other iv delivered reinforcers (Pickens et al. 1978). While this is in general agreement with the findings of Hanson et al. (1979) there are several differences between the results of the two studies. Hanson et al. (1979) reported that

across a 30 day period rats increased the daily number of nicotine infusions. In contrast, a stable level of daily infusions was obtained in the present study in 18 (± 1.5 SEM) days. In addition, Hanson et al. (1979) reported that following substitution of saline for nicotine there was a gradual increase (2 days) followed by a gradual decrease (4-6 days) in lever pressing. In the present study a similar pattern occurred but the time course was within 24 h. The difference in extinction rates between the two studies may be a result of the ability of nicotine to exert stimulus control of behavior when infused over a long (13 s) period of time (Hanson et al. 1979) vs a relatively short (4 s) infusions interval as used in the present study. This possible explanation must be qualified since in the Hanson et al. (1979) study albino rats were studied, they received programmed nicotine infusions for several days and a between groups design was used.

The result of delivering noncontingent infusions was a decrease in the number of response contingent infusions. However, the daily number of infusions (noncontingent + contingent) was stable across the four programmed interinfusion intervals. These data combined with the stable number of infusions across five ratio values (Fig. 4) suggest that under the present conditions the daily level of nicotine self-administration is at least in part under control of some tissue level of nicotine.

Nicotine-maintained lever pressing was studied over a range of doses in 7 rats. As the dose of nicotine was decreased responding increased then decreased resulting in an inverted V shaped dose-response function. The general relationship between magnitude of reinforcer and frequency of responding found in the present study was similar to that obtained with other reinforcers (Reynolds 1958; Goldberg 1973; Griffiths et al. 1979; DeNoble et al. 1981). In contrast to the inverted V shaped dose-response function, the nicotine intake (mg/kg of body weight) increased directly as a function of dose. At the maximum daily intake (3.2 mg/kg) the rats did not show any signs of toxicity as noted by Hanson et al. (1979).

Mecamylamine is an effective and specific antagonist for the behavioral effects of nicotine. Presession treatment with mecamylamine has been shown to antagonize both the rate-increasing and the rate-decreasing effects of nicotine when behavior was maintained in rats or squirrel monkeys under a FI and FR schedule of food presentation, water presentation or termination of a stimulus associated with electric shock (Morrison et al. 1969; Stitzer et al. 1970; Spealman and Goldberg 1982). Mecamylamine has also been used to antagonize the discriminative stimulus effect of nicotine in rats (Schecter and Rosecrans 1972; Hirshorn and Rosecrans 1974; Meltzer et al. 1980;) and antagonize the effects of intraventricular infusions of nicotine on behavior maintained under FR schedules of food presentation (DeNoble et al. 1982). When behavior of squirrel monkeys or dogs was maintained under FI sched-

ules (Spealman and Goldberg 1982) or FR schedules (Riser and Goldberg 1983) of iv nicotine infusions, presession treatment with 1.0 mg/kg of mecamylamine reduced responding maintained by nicotine infusions to saline-control levels. Infusions of nicotine (iv) and the delivery of electric shock both serve as punishers to suppress food maintained lever pressing in squirrel monkeys (Goldberg and Spealman 1983). Presession treatment with 0.1 to 0.3 mg/kg of mecamylamine reversed the suppression of responding produced by nicotine but did not alter the suppression produced by electric shock. In the present experiment, mecamylamine was also an effective antagonist of the behavioral effects of nicotine. When mecamylamine was administered at the beginning of a session, responding maintained by nicotine infusions was reduced and the amount of reduction was directly related to the mecamylamine dose. In contrast nicotine maintained responding in the same rats was not altered by presession treatment with hexamethonium. This combined with previous reports would suggest that the behavioral effects of nicotine are mediated by nicotine's effects on the central nicotinic receptors.

Opioid antagonists have been shown to reduce the intake of positive reinforcers such as food, water and ethanol (Marquies et al. 1970; Holtzman 1974; Altschuler et al. 1980). The reduction does not appear to be related to an abstinence syndrome, or of a general suppression of behavior (Stein and Belluzzi 1979), unless high doses (>5.0 mg/kg) of the antagonist are used (Segal et al. 1979). Naloxone has also been shown to reduce the amount of cigarettes smoked during a 3 h test per-

iod (Karras and Kane 1980). In contrast, naloxone has not been shown to be an effective antagonist of nicotine-induced antinociception in rats (Sahley et al. 1977; Tripathi et al. 1982). The present results are consistent with previous findings in rats in that naloxone across a range of doses was ineffective as an antagonist to the positive reinforcing effects of iv nicotine in rats.

To summarize, previous attempts to establish nicotine as an iv delivered reinforcer for rats have shown that only under conditions of reduced body weight and/or concurrent fixed-time food presentation or following programmed nicotine infusions will nicotine self-administration occur at rates above vehicle control levels (Lang et al. 1977; Hanson et al 1979; Lang and Smith 1980). The present results show that nicotine can function as an intravenously delivered positive reinforcer for rats in the absence of such conditions, and that the level of responding can be maintained across several ratio values. In this study the maintenance of lever pressing was unequivocally the result of consequent nicotine infusions. The fact that pretreatment with mecamylamine (a centrally-active nicotinic antagonist) but not hexamethonium (a nicotinic antagonist that does not readily penetrate the central nervous system) blocked the positive reinforcing effects of nicotine suggests that this effect is centrally mediated. In addition, the failure of large doses (3.0 mg/kg) of naloxone to alter the reinforcing effects of nicotine suggests that the endogenous opioid system may not mediate the effects. Furthermore, the behavior was shown to be sensitive to both dose and response contingency manipulations.

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Figure 1. Number of infusions (32 µg/kg/infusion) as a function of the number of days of access to nicotine for two individual rats. The solid line shows the rat with the longest acquisition time and the dashed line shows the rat with the shortest acquisition time. The open circle shows the average acquisition time for all 18 rats ± standard error.

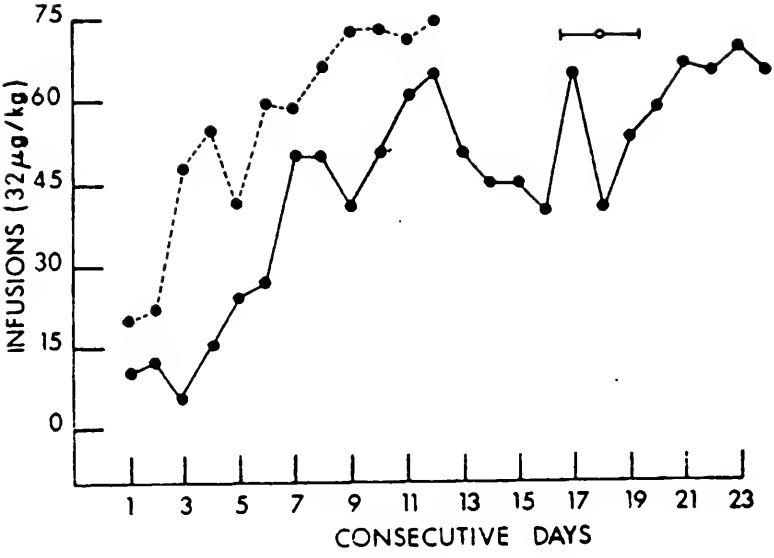
Figure 2. Number of infusions (left panel) and the session intake (right panel, mg/kg/session) as a function of varying the dose of nicotine under an FR 1 schedule. Nicotine doses were presented in a descending order. Each point is a mean of 21 sessions (7 rats x 3 sessions) and the vertical lines show the standard error.

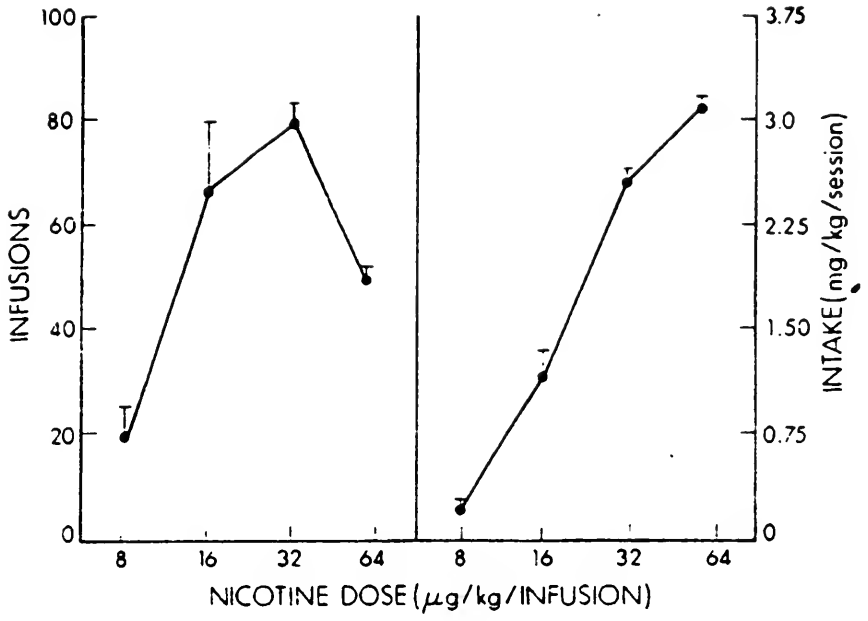
Figure 3. The average number of self-administered (solid line) infusions (32 µg/kg/infusion) and the total number of infusions (programmed + response contingent, dashed line) as a function of the interval between response independent nicotine infusions. Each point is the average of 3 rats and the vertical lines show the standard error. Points above control show the average numberof infusions with no programmed infusions.

Figure 4. The number of lever presses (solid line) and infusions (32 ug/kg dashed line) is shown as a function of the FR size. The ratios were presented in an ascending order. Each point is a mean of 9 observations (3 rats x 3 sessions) and the vertical lines show the standard.

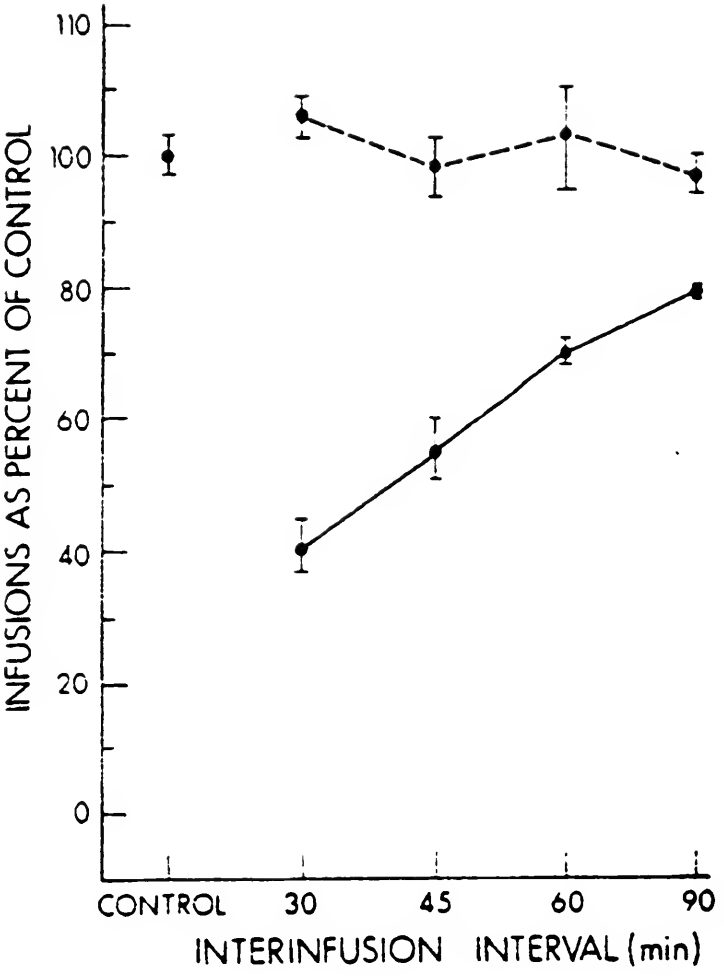
Figure 5. Effects of treatment with mecamylamine or hexamethonium on responding maintained by iv nicotine infusions in 4 rats maintained under a FR 1 schedule. Abscissa: dose of mecamylamine or hexamethonium given sc. The 0 dose consisted of the saline pretreatments (see Methods). Filled bars represent the number of infusions occurring during the 24 h session immediately following a mecamylamine injection. The number of infusions that occurred during the 24 h following a hexamethonium injection (1.5 and 3.0 mg/kg/sc) are represented by the dashed lines within the bars. Each bar is an average of 4 rats. The vertical lines show the standard error of the mean.

Figure 6. The average number of infusions in 3 hour blocks is presented for 3 saline (solid lines) and the 3 mecamylamine pretreatments (0.75 large dashed lines, 1.5 small dashed lines and 3.0 mg/kg/sc open circles) for 4 rats. The largest standard error for any 3 h period during the saline pretreatments was 2.12 infusions.

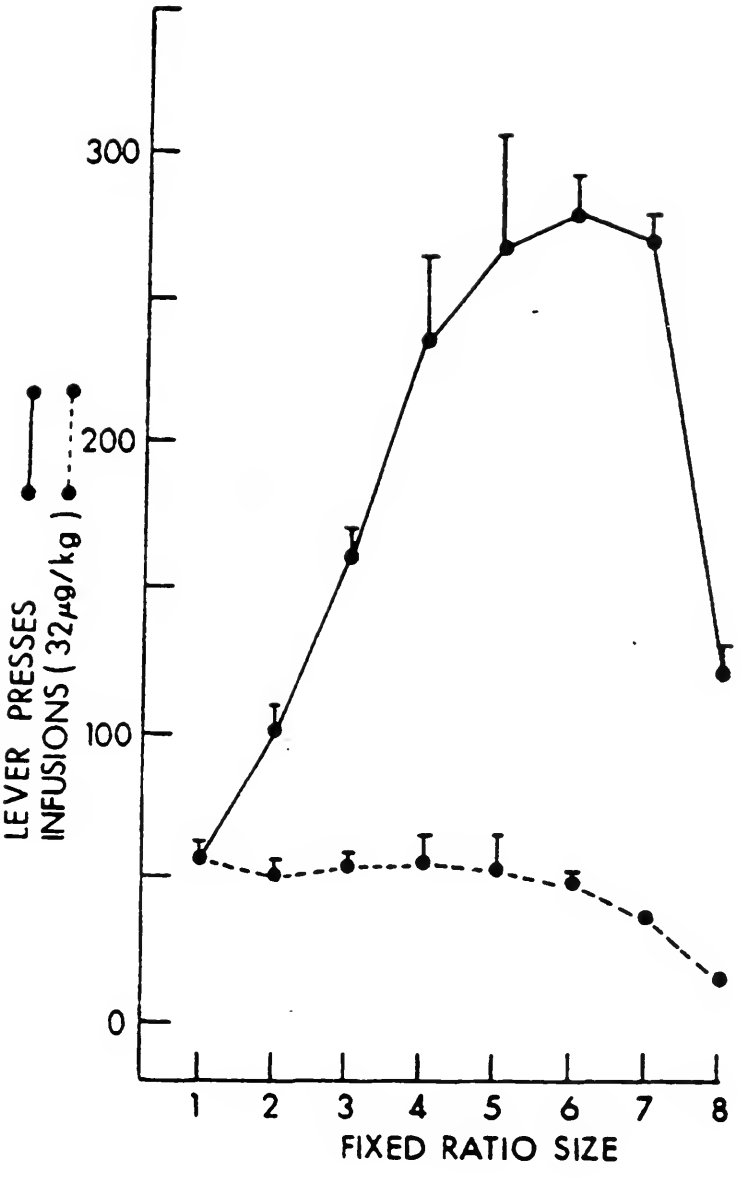

75
60
45
30
15
0
INFUSIONS (32µg/kg)
1
3
5
7
9
11
13
15
17
19
21
23
CONSECUTIVE DAYS


100
80
60
40
20
0
INFUSIONS
3.75
3.0
2.25
1.50
0.75
0
INTAKE (mg/kg/session)
8
16
32
64
8
16
32
64
NICOTINE DOSE (μg/kg/INFUSION)

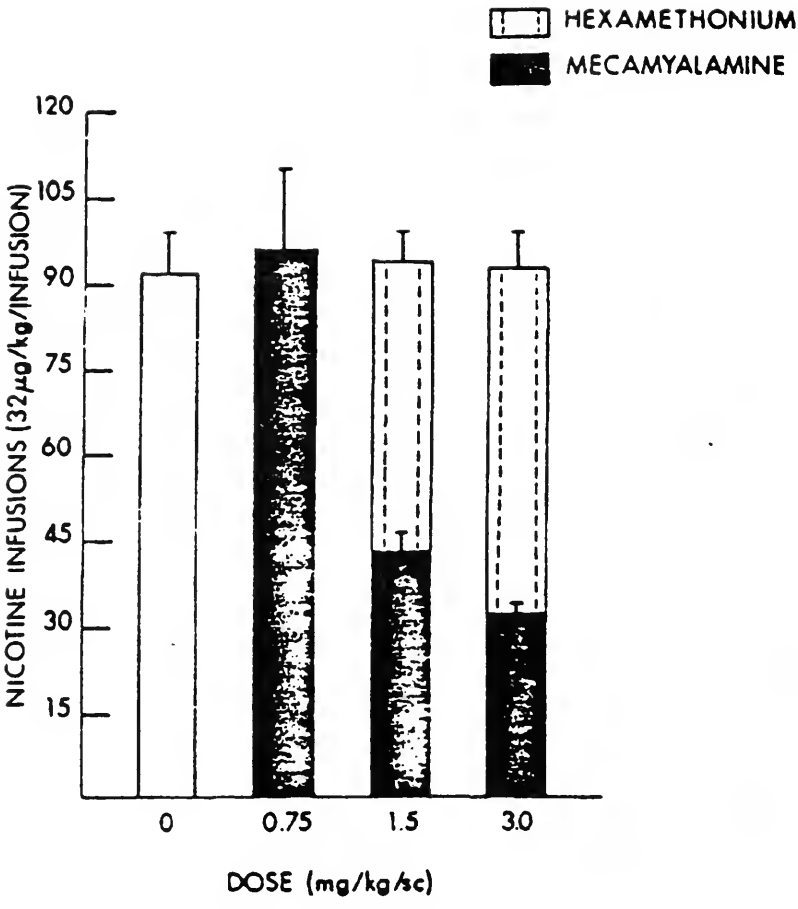
2


110
100
80
60
40
20
0
INFUSIONS AS PERCENT OF CONTROL
CONTROL
30
45
60
90
INTERINFUSION INTERVAL (min)

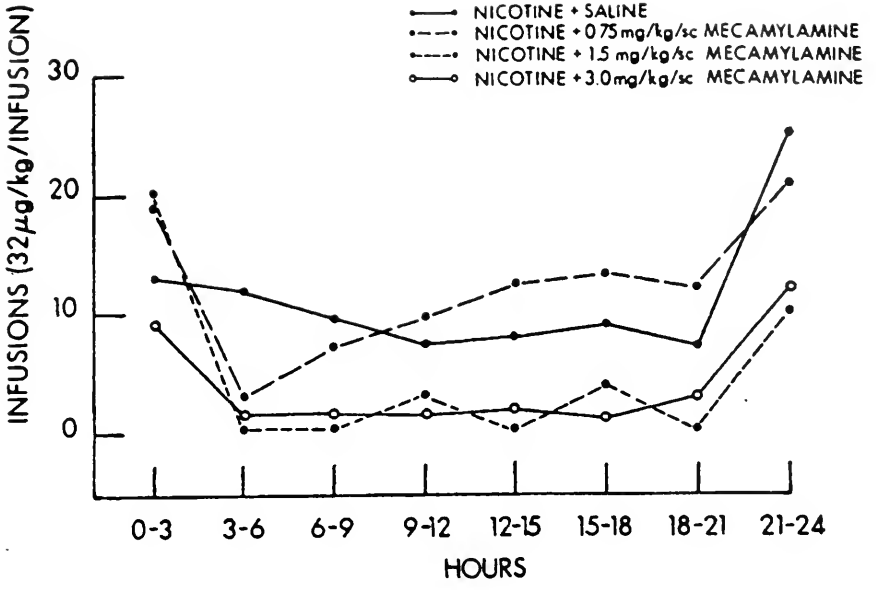
3


300
200
100
0
LEVER PRESSES
INFUSIONS (32μg/kg)
1
2
3
4
5
6
7
8
FIXED RATIO SIZE

4


HEXAMETHONIUM
MECAMYALAMINE
NICOTINE INFUSIONS (32µg/kg/INFUSION)
120
105
90
75
60
45
30
15
0
0.75
1.5
3.0
DOSE (mg/kg/sc)

5


NICOTINE + SALINE
NICOTINE + 0.75 mg/kg/sc MECAMYLAMINE
NICOTINE + 1.5 mg/kg/sc MECAMYLAMINE
NICOTINE + 3.0 mg/kg/sc MECAMYLAMINE
INFUSIONS (32μg/kg/INFUSION)
30
20
10
0
0-3
3-6
6-9
9-12
12-15
15-18
18-21
21-24
HOURS

6

Mr. SYNAR. This article is a revised version of a self-administration paper that Philip Morris suppressed in 1983. I understand that you sent that self-administration paper to the journal in December of 1985, without first getting a consent from Philip Morris. Some might say that this was a violation of your secrecy agreement. Did you take that risk?

Mr. DENOBLE. Yes, I did.

Mr. SYNAR. And why did you take that risk?

Mr. DENOBLE. It's one thing for industry to hold back scientific information because they are involved in the development of a product. It's another thing to say, we need to get the patents done.

It's done all the time in the drug industry. Scientists aren't free to publish right away. Usually, you have to get the product out, or you have to get a position in the marketplace. There are valid reasons to do that for market reasons.

This had nothing to do with the product. This information wasn't going out simply because the company didn't like what it said, and that was unacceptable. In 1986, people still weren't close to doing these kinds of research. They still hadn't picked up, so we took the risk.

Mr. SYNAR. I understand that in April of 1986, you and Dr. Mele went to St. Louis to present a paper on tolerance to nicotine before the Federation of American Societies for Experimental Biology. What was the response by Philip Morris to that?

Mr. DENOBLE. They sent us a letter indicating that was a violation of our agreement and that they would not tolerate that kind of conduct in the future.

Mr. SYNAR. I'd like to enter into the record as Exhibit 15, a copy of that letter.

Mr. WAXMAN. Without objection, it will made part of the record.

[Exhibit 15 follows:]

PHILIP MORRIS COMPANIES, INC.,
120 Park Avenue, New York, NY, April 23, 1986.

Dr. Paul C. Mele,
3205 Whispering Pines Drive, Silver Spring, MD

DEAR DR. MELE: It has come to our attention that you presented a paper at the Federation of American Societies for Experimental Biology in St. Louis on "The Development of Behavioral Tolerance Following Chronic Nicotine Administration." As you are aware, upon your employment at Philip Morris on November 16, 1981, you signed an agreement (a copy of which is enclosed) requiring you to keep confidential, unless expressly permitted otherwise, research developed while an employee of the Company. The disclosure of such information as a result of your employment at Philip Morris without permission constitutes a breach of your agreement with the Company. In the future, you are expected to comply with the terms of the agreement.

If you have any questions regarding this letter or the agreement, please address them to my attention.

Very truly yours,

ERIC A. TAUSSIG, ASSISTANT GENERAL COUNSEL.

Mr. SYNAR. Dr. DeNoble, I understand that in August of 1983, you and Dr. Mele spoke at a convention of the American Psychological Association in Washington, DC about another aspect of your work for Philip Morris. What was Philip Morris' response to that appearance?

Mr. DENOBLE. That was quite interesting because they actually had somebody out there taking pictures of us. They sent one of their people out to take a picture, and they sent us another letter

indicating that—a little stronger this time—action would be taken against us.

At that point, I called Mr. Taussig, who was, I think, the assistant general counsel, to discuss with him, to actually kind of let him know that we had submitted two manuscripts for review, and one was going to be published, and the other one was accepted and was going to be published. And that led to him telling me that if these articles were published, they would be suing us, and it would be very long and costly.

Mr. SYNAR. So that was the action to be taken? They were going to sue you?

Mr. DENOBLE. That is correct. They also indicated that if they could, they would try to bring an injunction against the journal to prevent publication of the self-administration paper. But that did not occur because I was able to pull it out.

Mr. SYNAR. Was this in writing?

Mr. DENOBLE. No, sir, it was not. It was in a phone conversation.

Mr. SYNAR. OK. I have a copy of that letter sent to you and Dr. Mele, dated September 10th, Exhibit 16. I'd ask unanimous consent that it be made part of the record.

Mr. WAXMAN. Without objection, that will be the order.

[Exhibit 16 follows:]

PHILIP MORRIS COMPANIES, INC.,
120 Park Avenue, New York, NY, September 10, 1986.

Dr. Victor J. DeNoble,
5603 Fox Run Drive, Plainsboro, NJ

Dr. Paul C. Mele,
3205 Whispering Pines Drive, Silver Spring, MD

GENTLEMEN: On April 23, 1986, I sent each of you a letter advising you of your obligations pursuant to the agreement which you signed with the Company at the commencement of your employment. In that letter, I indicated that the Company expected you to comply with the agreement. I also advised you that the Company considered your presentation of a paper at the Federation of American Societies for Experimental Biology in St. Louis in April 1986 based upon research performed at Philip Morris during the course of your employment to be a breach of the agreement since the consent of the Company had not been obtained.

We have since learned that during the latter part of August, you attended an American Psychological Association meeting in Washington, DC at which time you disclosed information relating to research on a project entitled "Brain Sites Involved in the Mediation of the Behavioral Effects of Intraventricularly Administered Nicotine." Management has determined that the research relating to this latest presentation was performed at Philip Morris. Again, the consent of the Company was not obtained.

The Company cannot tolerate this kind of conduct. As I stated in my earlier letter, if you wish to publish or otherwise utilize research from Philip Morris, you must request and receive permission from the Company. Any further breach of your agreement will result in action being taken.

Very truly yours,

ERIC A. TAUSSIG, ASSISTANT GENERAL COUNSEL.

Mr. SYNAR. Doctor, in this letter that you have before you, Philip Morris says, and I quote, "The company cannot tolerate this type of conduct. Any further breach of your agreement will result in action being taken." And that was signed by Eric Taussig, the assistant general counsel for Philip Morris. So what happened next was that he called you and then——

Mr. DENOBLE. No, sir. I called him to let—because when I got this letter, we had already sent out two more publications. I called him to let him know that they had gone out.

Mr. SYNAR. And you got a harsh lecture, based upon that conversation?

Mr. DENOBLE. Yes, sir.

Mr. SYNAR. Based upon that conversation, did you contact the psychopharmacological magazine to see what you could do?

Mr. DENOBLE. Yes, I called Herb Barry up and asked him what the status of the two papers were. The first paper, which was a brain site paper, had already gone to press. It was out, there was nothing we could do.

The self-administration paper, I believe your Exhibit 14, was in press but it had not gone to proof, so we were able to again, for the second time in 3 years, unfortunately, tell Herb that we had to pull the paper back.

Mr. SYNAR. All right. I have a copy of the letter that you sent the journal editor, Herbert Barry. It's Exhibit 17. I'd ask unanimous consent that it be made part of the record.

Mr. WAXMAN. Without objection, that will be the order.

[Exhibit 17 follows:]

September 22, 1986.

Victor J. DeNoble, Ph.D.,
Ayerat Laboratories Research, Inc., CW 8000, Princeton, NJ

DEAR VICTOR: The revised version of your MS 868-1666, received August 4, is satisfactorily improved and abbreviated. Thanks for your thorough, effective changes.

My routine check for discrepancies between the reference list and citations in the text has revealed that Lang et al. (1977) cited on pages 3 and 11, is not in the reference list. Since it was in the reference list in the prior version, this one of the 16 reference list items deleted apparently should have been retained.

I share the distress you expressed in your phone conversation of September 18 that the Philip Morris Company has issued an injunction against publication of this paper. I am returning to you the typescript, including the glossy prints of the four figures. I will accept your paper for publication and send it to the Technical Editor only if I receive from you a corrected typescript with the information that the injunction has been lifted.

When I return to the author a manuscript that I expect will be acceptable after revision, I keep it in a pending status for 6 months. At the end of that time, I send to the Journal's Production Office a circulation slip specifying that the paper will not be published. I will follow this procedure unless I receive contrary instructions from you.

Although it is disappointing both for you and for me that the efforts on this paper by you, by two expert reviewers, and to a lesser extent by me will apparently not result in publication, I believe that your effort and experience will be beneficially applied to your future papers. You have my best wishes for success in your ongoing and future research, and for useful publications reporting your findings.

Sincerely yours,

HERBERT BERRY, III, PH.D., FIELD EDITOR FOR BEHAVIORAL PHARMACOLOGY IN LABORATORY ANIMALS.

Mr. SYNAR. Now, this was a letter from Barry to you, and I want to quote from it. Quote, "I share the distress you expressed in your phone conversation of the 18th of September, that the Philip Morris Company has issued an injunction against the publication of this paper."

Dr. DeNoble, you have worked for other companies since Philip Morris, how do you compare these types of actions, which we have just detailed and the company's efforts to keep your work confidential with other companies you've worked with?

Mr. DENOBLE. Before I answer, let me just say that there is an error in the letter. The company never issued an injunction. They just told me they would, if I couldn't get it out. So that's an error.

I have never had this happen to me. I've never heard of it happening to any other scientist that I've ever talked to. This is very, very unusual. Paul? I don't know if Paul has. But I don't know if anyone else has tested the waters and gone against an agreement like this, like we signed. I mean, that was clearly——

Mr. SYNAR. Well, let's talk about that agreement, because you obviously have a confidentiality agreement. The last 10 years you haven't been free to talk publicly about your work. There have got to be other researchers in that same situation. How do these agreements work in practice? Are they, in effect, a complete bar to getting information to the very people that the information is supposed to serve?

Mr. DENOBLE. I've never had an agreement—I've never had an agreement with anybody else like this. This is the only agreement that I've ever had.

Mr. SYNAR. This is unique to the tobacco industry?

Mr. DENOBLE. No, sir, it's not. Industry has agreements that you will not divulge proprietary information, that you will not take data with you when you leave. Those every company has. This agreement was probably similar to those agreements, but it was being enforced in quite a different way.

This was used to prevent us from publishing information that did not relate to a product, did not relate to a marketing issue. It just didn't relate to anything like that. It was just the science. And what we found wasn't liked.

Mr. SYNAR. Let me conclude with just this general question, Dr. DeNoble, if I could. You are presently employed where?

Mr. DENOBLE. I work with the Department of Mental Retardation with the State of Delaware, servicing folks who have--or citizens who are mentally retarded.

Mr. SYNAR. And Dr. Mele, you are where?

Mr. MELE. I work with the Defense Department.

Mr. SYNAR. OK. What has this experience over the years told you about the tobacco industry? What does it tell you about the character and the trustworthiness of this industry?

More importantly, what did it feel like on April 14, 1994, as you watched as the rest of America did, the testimony of the seven chief tobacco executives of this country on the issue of whether or not, one, tobacco is deadly; and second, that nicotine is not addictive. What did you feel like at the moment when you saw that?

Mr. DENOBLE. That's a very difficult question to answer. You know, when I first agreed to appear before this committee, I promised that I probably would not go out and make public policy. It's difficult to watch those hearings and to feel good about what happened to us.

I would very much like to stick with the issues surrounding the laboratory, and would very much like to stick to the issues in the data, and would very much not like to personalize this. That's the best answer I can give you, sir.

Mr. SYNAR. Dr. Mele?

Mr. MELE. It just brought back to me the amount of data and type of data that we had collected and that was going nowhere. And in a very limited sense, that data should be out. I don't know

about broader public policy issues, but we put a lot of effort into collecting that data.

They asked us to collect it, they suppressed it, and it remains suppressed right now. It may be of use to the world, it may not. That should be put out and let the scientific community judge.

Mr. SYNAR. Thank you both.

Mr. WAXMAN. Mr. Synar, if you'll just yield to me. Not only did they suppress the data, but due to these agreements they had with you as researchers, and I assume they have this with all their researchers, they have been able to keep people who work for them from coming forward to talk about what they know and what they've done even as employees of the tobacco industry.

I want to tell you that I think you have come to us in good conscience, concern, and with a great deal of courage to make this presentation. And I hope others will be coming forward as well. Mr. Wyden?

Mr. WYDEN. Mr. Chairman, thank you. I'm going to go back to the laboratory in just a second, Dr. DeNoble.

But, Mr. Chairman, I would like to enter into the record at this point a Wall Street Journal article, February 11, 1993.

Mr. WAXMAN. Without objection, it will be put into the record.

[The article follows:]

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Smoke and Mirrors

How Cigarette Makers Keep Health Question 'Open' Year After Year

Council for Tobacco Research Is Billed as Independent But Guided by Lawyers

An Industry Insurance Policy

By Alix M. Freedman
And Laurie P. Cohen
Staff Reporters of The Wall Street Journal

This is the story of the longest-running misinformation campaign in U.S. business history, and how it may ultimately backfire on its corporate sponsors.

The tale opens in 1954. Cigarette smoking, like tail fins and the new music called rock-and-roll, was fun and glamorous. But a warning had just been sounded that smoking might not be good for you. A scientist at Memorial Sloan-Kettering Cancer Center had painted tobacco tars on the backs of mice and produced tumors. The tobacco industry met this sudden threat head-on.

In full-page newspaper ads headlined "A Frank Statement to Cigarette Smokers," tobacco companies announced that a new research group, funded by the industry but independent, would examine "all phases of tobacco use and health." Its solemn pledge: "We accept an interest in people's health as a basic responsibility, paramount to every other consideration in our business."

The tobacco industry's main vehicle for damage control was up and running.

Sowing Doubt

For almost four decades, the Council for Tobacco Research in New York has been the hub of a massive effort to cast doubt on the links between smoking and disease. Sponsored by U.S. tobacco companies and long run behind the scenes by tobacco-industry lawyers, the ostensibly independent council has spent millions of dollars advancing sympathetic science. At the same time, it has sometimes disregarded, or even cut off, studies of its own that implicated smoking as a health hazard.

"When CTR researchers found out that cigarettes were bad and it was better not to smoke, we didn't publicize that" in press releases, says Dorothea Cohen, who for 24 years until her retirement in 1989 wrote summaries of grantee research for the Council's annual report. "The CTR is just a lobbying thing. We were lobbying for cigarettes."

Many companies under attack for their products have underwritten research to buttress safety claims. What sets the tobacco industry apart is the scope, aggressiveness and persistence of its undertaking. For decades rival tobacco companies have acted in concert to combat the growing body of evidence linking their products to cancer, heart disease and emphysema.

Cheap Insurance

The U.S. Centers for Disease Control today links 434,000 deaths a year to smoking. The surgeon general has declared smoking "the single largest preventable cause of death and disability," citing "overwhelming" evidence from no less than 50,000 studies. Yet the wisp of uncertainty supplied by the Council has always been enough to protect the $50 billion industry in Congress and especially in court, and tobacco companies have never paid a dime in product liability claims.

Addison Yeaman, a former Brown & Williamson Co. lawyer and ex-chairman of the Council, says the passage of time hasn't altered his faith in this view expressed at a Council meeting in 1975: The "CTR is (the) best and cheapest insurance the tobacco industry can buy, and without it, the industry would have to invent CTR or would be dead."

Michael Pertschuk, a former chairman of the Federal Trade Commission, finds the industry's defense extraordinary: "There never has been a health hazard so perfectly proven as smoking, and it is a measure of the Council's success that it is able to create the illusion of controversy in what is so elegantly a closed scientific case."

A Legal Peril

But now the device the industry has so long used to deflect attack has become its biggest vulnerability. That is because the Supreme Court last year said smokers can sue, accusing the industry of deliberately hiding or distorting smoking's dangers. And the U.S. attorney's office in Brooklyn, N.Y., is conducting a criminal investigation into whether the industry used the Council to defraud the public.

Whether anything will come of the criminal inquiry — and whether plaintiffs can convince juries that the industry did in fact misrepresent health hazards — are very much open questions; just last month, one jury rejected allegations of a conspiracy. But if plaintiffs should begin to succeed, perhaps by gaining access to now-secret Council documents, they could turn on its head what up to now has been an almost totally winning industry strategy.

The Council for Tobacco Research declined to respond to questions about its activities, as did all of the Big Six tobacco companies — Philip Morris Cos., RJR Nabisco Holdings Corp., American Brands Inc., B.A.T. Industries PLC (parent of Brown & Williamson), Loews Corp. (parent of Lorillard) and Brooke Group Ltd. (parent of Liggett Group).

At the outset, many in the industry thought the late-1953 crisis posed by the Sloan-Kettering mouse research was entirely manageable. With the Council, "the industry was told that in the best of worlds, we'd do a great service to mankind," says James Bowling, a former Philip Morris director. "Our product either would be exonerated or, if involved (in causing cancer), they'd identify the ingredients and we'd take them out. We thought this was marvelous."

So apparently did some scientists. The Council snagged a noted figure, Clarence Cook Little, as its scientific director. Thanks to his renown as a former University of Michigan presi-

dent and director of a prestigious laboratory, the Council was able to attract an illustrious scientific advisory board, which culled through proposals from a who's who of American scientists who sought its research grants. Over the years, it has doled out more than $200 million.

But the Council's role was never just research. It was largely a creature of Hill & Knowlton, the public relations firm, which cigarette merchants retained when the mouse research came out. Hill & Knowlton installed the Council in the Empire State Building in New York, one floor beneath its own offices, with one of the PR firm's staffers as the supposedly independent research council's executive director. Hill & Knowlton also began publishing a newsletter that reported such news items as "Lung Cancer Found in Non-Smoking Nuns," and it helped authors generate books with titles like "Smoke Without Fear" and "Go Ahead and Smoke."

Some people, including many in the news media, were skeptical of the Council. "To reporters, the Council was never independent," says Earl Ubell, a veteran science reporter at WCBS-TV in New York. "It was a wholly owned subsidiary of the tobacco industry." But in the interest of balance, journalists writing on smoking and health routinely included the Council's views.

And many smokers lacked the professional skepticism of reporters. "You would have to have lived in that era to understand — they kept providing false reassurances, so I had no idea that smoking was so very dangerous," says Janet Sackman, who once appeared in ads as Miss Lucky Strike and who now has throat cancer.

As early as 1958, however, the Council had strong intimations from studies it financed that smoking could be dangerous. "Cigarette smoke condensate is a weak mouse skin carcinogen," said a Council-financed study completed in that year.

Ensuing Council-financed research found more links to disease. In 1961, a study of 140 autopsies at a Veterans hospital in Iowa City, Iowa, said "a history of cigarette smoking is significantly related to the incidence of carcinoma." In 1963, researchers at Philadelphia General Hospital and the University of Pennsylvania linked chronic smoking to earlier coronary artery disease and a higher incidence of coronary occlusion.

The Council summarized such results in its annual reports, but it often chose other research to stress to the public. Ms. Cohen, who wrote the summaries, cites a 1965 study that said pregnant women who smoked had smaller babies and were more likely to give birth prematurely. But the industry in 1982 submitted to Congress a study the Council hadn't financed, saying that smokers had no greater risk of premature babies and that low birth weight wasn't a problem.

"In the '60s," says Ms. Cohen, "there was so much bad news about smoking that there really wasn't much the CTR could put out, but anything they could find they would use."

THE LAWYERS STEP IN

By 1964, keeping the case open was no longer just shrewd public relations; it had become a legal imperative. As more Americans came to believe smoking could kill, the number of tobacco liability suits jumped to 17 from seven the year before. And in that year, the Surgeon General labeled smoking a health hazard.

It "was a serious, stunning shock," says Mr. Bowling, the former Phillip Morris director. "That's the stage at which the lawyers became a lot more involved."

Needing a defense from science as never before, yet dreading the legal exposure that adverse research would bring, the industry created within the Council a Special Projects division — with lawyers, not scientists, at the helm. Much of what it did was shrouded in mystery. "Everything was cloak-and-dagger," recalls John Kreisher, a former associate scientific director of the Council. "We weren't allowed on their floor."

The core of the lawyers' operation was a vast database, storing the world's literature on tobacco and health, data on foes and strategy documents. The lawyers began shuttling the globe, looking for research and expert witnesses. They sought out studies supporting causation of lung cancer by factors other than smoking and research suggesting the complex origin of all diseases linked to tobacco.

Overtures to scientists usually were handled by outside law firms, especially Jacob, Medinger, Finnegan & Hart in New York. It also served as counsel to the Council, and its Edwin Jacob took the lead role at the Special Projects unit. This arrangement offered crucial advantages. Notes Roy Morse, a former research chief at R.J. Reynolds: "As soon as Mr. Jacob funded" a scientific study, "it was a privileged relationship and it couldn't come into court" because of legal rules protecting attorney-client communications. "So they could do projects that they could bury if they chose."

How often they may have done that is unclear, because 1,500 Council documents are under seal in a federal suit in New Jersey, withheld under the attorney-client privilege. In any case, the industry had other options, such as halting funding after an initial phase. Mr. Jacob and the firm of Jacob Medinger declined to comment.

SCIENTISTS SIGN UP

In 1972, the Special Projects unit gave Hugh Fudenberg, an immunologist, funding to determine whether some people are genetically predisposed to emphysema. Early results indicated up to 10% might be. Dr. Fudenberg planned "to warn high-risk people not to smoke," he says, but before he could his funding was discontinued without explanation. "They may have cut me off because it would have been negative for them," he speculates.

A researcher named Geoffrey Ashton learned the limits of the Council's independence in 1976. He was invited by Mr. Jacob to study whether there might be some genetic factor underlying both smoking and certain diseases. But the study never got funded. Dr. Ashton says the lawyer told him "the presidents of the tobacco companies had turned down the proposal because they didn't think the outcome would be useful to them."

This case, like several others, points up the sometimes-perplexing relationship between scientists and the tobacco Council. Dr. Ashton says he was "very apprehensive" about casting his lot with the industry. What finally won him over? "Not to shock you, but scientists are always looking for money to further their research," Dr. Ashton says.

Likewise, a pharmacologist, Charles Puglia, did a special project for the Council's lawyers from 1979 to 1981, although he believed smoking to be dangerous. He explains: "It was early on in my career and it got me started with a laboratory."

While these scientists hesitated to accept tobacco funding but finally said yes, others, such as Theodore Finley, hesitated and finally said no. Dr. Finley, encouraged by Jacob Medinger lawyers to apply for cigarette research funding, decided to examine whether emphysema can result from a reduction that smokers face in a protective lining of the lung. He soon backed out. "If my theory was correct, it would have discredited cigarettes," he says. "But it would be hard to talk about the evils of tobacco while being supported by them at the same time. This was dirty money — I felt like a prostitute."

The researchers the Council cultivated most assiduously were those of a different breed: contrarians whose work disputed the perils of tobacco. For instance, James F. Smith did two controversial studies in the 1960s and 1970s saying smoke-

ss tobacco did not cause cancer. (The surgeon general in 1986 said it raised the risk of oral cancer.)

Although Dr. Smith all but repudiated his own conclusions on CBS's "60 Minutes" in 1985 — urging the public to avoid smokeless tobacco — a short time later he acknowledged he accepted an offer of several thousand dollars from Jacob Medinger lawyers to review scientific literature in preparation for a tobacco liability suit. The plaintiff was the mother of an Oklahoma youth who had died of oral cancer after using smokeless tobacco for seven years.

The Jacob Medinger firm and other defense lawyers won the suit, invoking Dr. Smith's studies as independent research. But there are indications he had longstanding ties to the Council; one court document shows his first study was earmarked a "priority" for funding by Council lawyers 20 years earlier. Dr. Smith says the Council paid for equipment at his department's lab at the University of Tennessee when he was doing his smokeless tobacco studies, though it didn't finance the studies.

REWARDING RESEARCH

Two other favorite scientists of the Council were Carl Seltzer and Theodore Sterling. Dr. Seltzer, a biological anthropologist, believes smoking has no role in heart disease and has alleged in print that data in the huge 45-year, 10,000-person Framingham Heart Study — which found otherwise — have been distorted by antitobacco researchers. Framingham Director William Castelli scoffs at Dr. Seltzer's critique but says it "has had some impact in keeping the debate alive."

Dr. Sterling, a statistician, disputes the validity of population studies linking smoking to illness, arguing that their narrow focus on smoking obscures the more likely disease cause — occupational exposure to toxic fumes.

For both men, defying conventional wisdom has been rewarding. Dr. Seltzer says he has received "well over $1 million" from the Council for research. Dr. Sterling got $1.1 million for his Special Projects work in 1977-82, court records show.

In relying on such research, the tobacco industry is "exploiting the margins of science," contends Anthony Colucci, a former top researcher and later director of scientific litigation support at R.J. Reynolds. He offers an analogy: "There's a forest full of data that says tobacco kills people, and sitting on one tree is a lizard with a different biochemical and physiological makeup. The industry focuses on that lizard — that tiny bit of marginal evidence."

R.J. Reynolds is suing Dr. Colucci, an outspoken critic, to keep him from testifying in a trial or talking to the media about tobacco liability, and accuses him of demanding a big consulting contract to keep quiet. Dr. Colucci says Reynolds "manipulated the negotiations" so it can now portray them as an extortion attempt. He adds: "This is a clear demonstration of the extent to which a tobacco company will go to silence someone who is telling the truth."

The Special Projects unit worked in a variety of ways to protect tobacco companies. Lobbying in Congress against advertising curbs, the industry in 1982 submitted to Congress a researcher's statement that peer pressure, not advertising, induced young people to smoke. Congress wasn't told that the research had been funded by Council attorneys. This was no accident. At a meeting of tobacco-company lawyers the year before, Mr. Jacob explained that the reason for funding that particular research as a Special Project was to conceal the researcher's ties to the industry. "We did not want it out in the open," Mr. Jacob said, according to the meeting transcript as cited in a Newark, N.J., federal judge's opinion.

The Council's lawyers weren't content for long to confine their activities to the Special Projects division. By the late 1960s, they had begun to encroach on the smoking research emanating from the putatively independent Council itself. Often, the Council and its lawyers shared or swapped projects and scientists.

By 1968, the Council had begun putting researchers under contract for many studies. This gave it the right to control both a study's design and publication of the results. However, as a contractor, the Council could be held responsible for withholding negative findings. So its operatives would do their utmost to ensure that ugly surprises didn't arise.

This contributed to a parting of the ways with Hill & Knowlton. "The lawyers had this thing under control," recalls Loet Velmans, a former chief executive of the PR firm. It quit the account in the late 1960s, he says, out of frustration that the industry "for legal reasons felt it couldn't admit to anything (on tobacco and health) because then it would be sued out of existence."

Says Robert Kersey, a former head of tobacco research at Liggett: "Almost everything that transpired had to be done under the advice of counsel so that nothing . . . would incur a potential liability."

SMOKING RODENTS

In 1968, the Council contracted with Mason Research Institute in Worcester, Mass., to evaluate "smoking machines" for animal inhalation studies and do toxicity tests on rodents. As the study drew to a close in 1972, Mason researcher Miasnig Hagopian was astonished when scientists from the Council and from R.J. Reynolds began turning up weekly at his lab, where he says they sat for hours taking notes. They made sure that only the most genetically vigorous (that is, cancer-resistant) rodents were going to be used, he says, and dictated which cigarettes and how many puffs were administered to them.

"It got to the point where they were directing the course of the study," says Dr. Hagopian. "It was nowhere near as objective as if it had been funded by" the government.

Although he did complain to Mason's president, Dr. Hagoplan concedes he and other researchers mainly "looked the other way." They wanted to make sure the contract was renewed so they could do the critical experiments on whether smoke affects rodents' lung tissues. However, the Council canceled funding before Mason began the animal study.

The Council pulled out the big guns after another study, at Bio-Research Institute in Cambridge, Mass. When Syrian hamsters were exposed to smoke twice a day for 59 to 80 weeks, 40% of those of a cancer-susceptible strain and 4%of a resistant strain developed malignant tumors. Before publishing the study in 1974, the institute's founder, Freddy Homberger, sent a manuscript to Robert Hockett, then scientific director of the Council. Dr. Homberger says he had to do so because halfway through his study, the Council had changed it from a grant to a contract "so they could control publication — they were quite open about that."

Soon thereafter, Dr. Hockett and Mr. Jacob, the lawyer, hastened to Dr. Homberger's summer home in Maine. Their mission? "They didn't want us to call anything cancer," Dr. Homberger testified years later at the Rose Cipollone tobacco liability trial in federal court in Newark, N.J. "They wanted it to be pseudo-epitheliomatous hyperplasia, and that is a euphemism for lesions preceding cancer. And we said no, this isn't right. It is a cancer." Today, Dr. Homberger adds that Mr. Jacob told him he would "never get a penny more" if the paper was published without making the changes.

He compromised. At the last minute, he changed the final proofs to read "micro-invasive" cancer, meaning a microscopic

malignancy. Despite this, his lab was never funded by the Council again.

Dr. Homberger would come to regret his concession. And the Council would find a use for it — on the same occasion on which it eventually would use research from another lab, Microbiological Associates of Bethesda, Md.

WHAT KIND OF CANCER?

The Council contracted with that lab to do the world's largest inhalation study, involving more than 10,000 mice. To do it, the Council spent hundreds of thousands of dollars in a quest for the perfect smoking machine, one that prevented mice from either holding their breath or overdosing on carbon monoxide. The lab initially had considered freedom, says Carol Henry, who was its director of inhalation toxicology. But after nine years of work and $12 million, the team was told in 1982 that it could no longer meet with Council staffers unless a lawyer was present.

"We had never done science through lawyers before, and we told them it was unacceptable," says Dr. Henry. She says a Jacob Medinger lawyer told her, "That's the way it is."

The scientists knuckled under. If the Council had canceled before all phases of the first experiment were done, 40 staffers might lose their jobs and nine years' worth of data would never come to light.

In the first experiment, in which mice inhaled the equivalent of five cigarettes a day, five days a week, for 110 weeks, 19 out of 978 mice got cancer — versus seven out of 651 controls. However, the tumors weren't squamous-cell carcinomas, the kind usually seen in human lung cancer. And there was a 10% possibility the results were due to chance, whereas scientists prefer no more than 5%. Even so, Dr. Henry says the study built a "very strong case" that cigarettes can induce cancers in animals. This was to be the first of several experiments.

But lawyers from Jacob Medinger told Microbiological the project would go no further. "When a contract is canceled given these kinds of results," Dr. Henry says, "reasonable scientists might conclude the liability issue must have suddenly become apparent to this group." In fact, says Dr. Kreisher, the Council's former associate scientific director, Council lawyers "worried like hell" about it.

Microbiological and the Council parted ways, but the tobacco industry got plenty of mileage out of the Microbiological mice. In 1984, the Council issued a news release noting the absence of squamous-cell lung cancer in the lab's study. The timing wasn't coincidental. That year lawyers from Liggett, Phillip Morris and Lorillard began taking depositions in the landmark case of Mrs. Cipollone, a New Jersey woman whose family claimed she had died of smoking-related squamous-cell lung cancer. And at the federal trial four years later, a witness for the defense said the fact that the smoking mice didn't get squamous-cell carcinoma (although some did get cancer) showed that "cigarette smoke has not been shown to be a cause of lung cancer."

The witness also put Dr. Homberger's Syrian hamsters to good use. Smoking hadn't produced any more than "microinvasive" tumors in the hamsters, noted the witness, toxicologist Arthur Furst.

Dr. Homberger, regretting he had agreed under pressure to use this milder wording, calls this use of his report "baloney," adding: "It was cancer beyond any question, not only in our opinion but in the view of the experts who looked at the slides." Dr. Furst declined to comment.

The tobacco companies succeeded in planting doubt in some jurors. "I didn't think it was proven scientifically that smoking caused her lung cancer," says juror Barbara Reilly. She says that under pressure from other jurors, she and two other holdouts went along with a finding in favor of the Cipollones, but managed to hold the damages to $400,000 instead of the $20 million some wanted to give. The award was based on false safety assurances by cigarette companies in their pre-1966 advertising.

An appeals court overturned the verdict, saying the plaintiffs had to prove Mrs. Cipollone had relied on the ad claims. In December, the Cipollones withdrew the suit rather then retry it, citing the cost.

The advent of this suit had coincided with the end of the Council's contract and Special Projects research, as well as the waning influence of Jacob Medinger, which departed under pressure in 1984. Tobacco industry lawyers say privately that executives and attorneys grew fearful that the Council, though designed to deflect liability, would wind up incurring just that, because it could be portrayed as having breached a public pledge to do independent research.

LEGAL LANDSCAPE SHIFTS

In fact, by the mid-1980s, the industry had begun to face the very suits against the Council that it feared. In one, the Cipollone family's lawyer, Marc Edell, sued the Council in 1984 on behalf of Susan Haines, the daughter of a lung-cancer victim.

To prove his claims of fraud and conspiracy, Mr. Edell has been trying to get access to the 1,500 Council documents the industry has kept secret by invoking attorney-client privilege. Such privilege can be abrogated in case of fraud, and last year a federal judge in Newark, citing possible evidence of fraud, set in motion the process of making documents available to Mr. Edell. The judge, H. Lee Sarokin, who had been hearing tobacco lawsuits for a decade, wrote a scathing opinion saying that the tobacco industry may be "the king of concealment and disinformation."

A federal appeals court removed him from the case last September for failing to maintain the appearance of impartiality. A new judge will decide the critical issue of whether the industry must divulge any of the 1,500 Council documents.

In the meantime, plaintiffs' attorneys are pinning their hopes on the Supreme Court's ruling last June. The ruling, which grew out of the Cipollone case, said that although cigarette warning labels prevent smokers from bringing "failure to warn" cases, plaintiffs may file suits alleging that cigarette makers intentionally hid or misrepresented tobacco's health hazards. This has led some to view the Council for Tobacco Research as the key to recovering damages from the industry.

But doing so may not be easy. At the end of January, a state court jury in Belleville, Ill., rejected the allegation that companies had conspired to play down tobacco's dangers. Some say winning such a case may depend on getting access to sealed Council documents.

Also facing an uphill battle is the criminal investigation by the U.S. Attorney in Brooklyn, N.Y. Prosecutors are facing statute-of-limitations problems because the Special Projects unit was disbanded more than five years ago.

But what may prove the best protection for the tobacco industry is the readiness of certain scientists to read the evidence differently from the majority. Says Dr. Colucci, the ex-Reynolds employee: "The scientists can come from Mars, but no matter how obscure or how misbegotten, as long as they are willing to tell the scientific lie that 'it's not proven,' the tobacco industry is off the hook." ■

Mr. WYDEN. This article makes it very clear that what Dr. DeNoble and his associate are talking about is not some kind of isolated case. What you are describing according to the Wall Street Journal, not exactly an organ of anti-business kind of thinking, has gone on on a number of occasions.

So I'm going to take you back to the laboratory, Dr. DeNoble, and I understand that you would be more comfortable there. But I think that the American people need to know that publications like the Wall Street Journal are outlining some specifics, the kinds of things that you've described very clearly today.

Mr. WAXMAN. If you'd yield to me because——

Mr. WYDEN. I'd be happy to yield.

Mr. WAXMAN. Some people may not have read that article, and I would recommend it to people to read it. But that article indicated a multi-decade period of effort by the tobacco industry to sponsor research and then to suppress research to make sure that what they knew didn't get out so they could always have that deniability.

There was not only deniability. They used their research findings to try to make things look as if they were still open questions rather than concluded scientific issues. And so I thank the gentleman for, again, raising that article, and I think it's appropriate to have it in the record.

Mr. WYDEN. Dr. DeNoble and Dr. Mele, let's talk about this matter of tolerance for nicotine. My sense is you all understand the science better than we do, of course. Tolerance implies when an animal or a human being gets a diminished effect with repeated doses of a drug, and it's one of the indicators of a potential abuse liability or addiction.

Now, Dr. Mele, I guess maybe we'll start with you on this. Did your work find that rats developed a tolerance to nicotine?

Mr. MELE. Yes, we did.

Mr. WYDEN. Now, we've got a manuscript that you wrote with Dr. DeNoble entitled, Development of Behavioral Tolerance Following Chronic Nicotine Administration.

Mr. Chairman, I would ask that this be entered into the record as well.

Mr. WAXMAN. Without objection, that will be the order.

[Testimony resumes on p. 123.]

[The paper follows:]

DEVELOPMENT OF BEHAVIORAL TOLLERANCE FOLLOWING CHRONIC NICOTINE ADMINISTRATION

Paul C. Mele and Victor J. DeNoble

It is well documented that tolerance develops to many of the effects of nicotine following its repeated administration. In humans, tolerance to the pressor and subjective effects of intravenously administered nicotine has been reported (Jones et al., 1978; Rosenberg et al., 1980). In rats and/or mice, tolerance develops to nicotine-induced convulsions (Behrend and Thieves, 1933), electroencephalographic arousal (Hubbard and Gohd, 1975), and increases in corticosterone secretion (Benwell and Balfour, 1979; Balfour, 1980) and in urinary catecholamine levels (Westfall and Brase, 1971). Behaviorally, tolerance develops to nicotine-induced suppression of locomotor activity (Behrend and Thieves, 1933; Falkenborn et al., 1981; Hatchel and Collins, 1977; Keenan and Johnson, 1972; Morrison and Stephenson, 1972; Stolerman et al., 1973; 1974) and responding maintained by fixed ratio (FR) schedules of reinforcement (Domino and Lutz, 1973; Dougherty et al., 1981; Hendry and Rosecrans, 1982). In contrast, feeding studies suggest that tolerance does not develop to the decreases in body weight and in food and fluid intake produced by nicotine (Baettig et al., 1980; Falkenborn et al., 1981).

For schedule-controlled responding, Domino and Lutz (1973) reported that the first administration of 0.25 mg/kg of nicotine suppressed lever pressing under and FR 15 schedule of water presentation for the majority of a 45 minutes test session; recovery of control response rates occurred rather abrubtly towards the end of the session. Daily injections of nicotine resulted in a progressive attentuation of the suppression. By day 15 of chronic dosing only a slight suppression of responding was evident at the start of the session. Dougherty et al., (1981) reported a similar finding using an FR 50 schedule. These investigators also demonstrated that once tolerance developed, suppres-

sion of responding was reinstated in a dose-dependent manner by higher doses of nicotine (0.35 - 0.65 mg/kg).

It is unclear whether the development of tolerance to the behaviorally disrupting effects of nicotine is due to altered concentrations of nicotine at the receptor (i.e., dispositional tolerance), to altered sensitivity of nicotine receptors (i.e., functional/physiological tolerance), or to certain behavioral or environmental factors (Dews, 1978; Schuster, 1978). A variety of compounds have been examined with a procedure designed to separate the influence of behavioral from dispositional and/or physiological mechanisms of tolerance (Campbell and Seiden, 1973; Carlton and Woglin, 1971; Chen, 1969; Harris and Snell, 1980; Le Blanc et al., 1976; Meltzer and Rosecrans, 1982; Murray et al., 1977; Woolverton and Balster, 1979). This procedure involves the chronic dosing of different groups of subjects either before or after the experimental session. The test performance of the group dosed before the session is therefore altered by the compound, whereas the performance of the group dosed after the session is not altered. Once tolerance develops in the group dosed before testing, the group dosed after testing is administered the compound presession as a test for tolerance. If the before group is found to be more tolerant than the after group, then it is implied that factors arising from the disruption of the test performance by the compound (and not the mere repeated administration of the compound) were instrumental in determining the extent to which tolerance developed.

While the present study was in progress Hendry and Rosecrans (1982) reported using the before/after paradigm to evaluate nicotine tolerance in mice responding under an FR 25 schedule of sweetened milk reinforcement. Acute nicotine suppressed responding in a dose-related manner (0.2 - 1.6 mg/kg/s.c.).

A dose of 1.2 mg/kg of nicotine which reduced response rates to 15% of control levels was then administered daily until tolerance developed in the before group. Responding in the after group was not affected by postsession injections of nicotine. When the nicotine dose-effect functions were redetermined while chronic dosing continued, the two groups of mice were found to be equally tolerant to the rate-decreasing effects of nicotine. These findings were interpreted as indicating that behavioral variables do not influence the development of tolerance to nicotine.

The present study used the before/after dosing paradigm to investigate whether behavioral factors may be involved in the development of tolerance to nicotine. In rats responding under an FR 32 food schedule, tolerance to the disruptive effects of nicotine developed with chronic dosing. Behavioral factors were found to be involved in the development of tolerance to nicotine, since the before group showed a significantly greater degree of tolerance than the after group when comparisons were made at several times during chronic dosing and once chronic dosing was terminated.

METHODS

Animals

Fourteen naive male Long-Evans hooded rats (Blue Spruce Farms, Altamont, N.Y.), 90-120 days old and weighing 325-350 g at the start of the experiment were used. The rats were maintained at approximately 85% of their ad libitum weights which was determined from the last five days of a two week free-feeding period; weights were maintained by restricted feedings with Purina Rodent Chow approximately 30 minutes after daily testing. Animals were singly housed in wire mesh cages in which water was always available. Temperature and humidity

were controlled and a 12 hour light (0700 to 1900 hrs) - dark cycle was in effect.

Apparatus

Four identical oprant conditioning chambers (Lehigh Valley Electronics No. 143-25), each contained a sound and light attenuating cubicle (LVE No. 132-02), were used. On one wall of the chamber were two levers (LVE No. 121-05), a pellet receptacle, six cue lights (lever lights), a speaker and a house light. A pellet dispenser delivered one 45 mg food pellet (Bio-Serve) with each operation. White noise was constantly present in the testing room and an exhaust fan mounted in each cubicle provided ventilation. Programming of experimental contingencies and recording of data were accomplished with the use of solid state logic module digital counter and cumulative recorders located in an adjoining room.

Procedure

Rats were tested initially in daily sessions under a fixed ratio 1 (FR 1) schedule for either 60 minutes or until the food pellets were delivered, whichever occurred first. There was no attempt to hand-shape the lever press response and all rats were responding reliably after a maximum of seven days. Food pellets were delivered for responses on the left lever only. Responses on the right lever had no programmed consequence but were recorded as a measure of general activity. After 2 - 3 sessions in which 100 food pellets were delivered under the FR 1 schedule, session duration was decreased to 30 minutes and the FR response requirement was gradually increased over a 2 to 4 week period until an FR 32 schedule was in effect. Responding under the FR 32 schedule stabilized after 4 to 6 weeks of testing daily, Monday through Friday.

Stability was defined as the absence of any consistent increasing trends in response rates over 10 consecutive sessions. Once responding stabilized, sterile 0.9% physiological saline injections were given once or twice per week for several weeks to adapt the animals to the injection procedure. Dose-effect functions for (-)-nicotine (nicotine hydrogen tartrate, Chemicals Procurement Laboratories Inc.) were then determined. (-)-Nicotine (0.5, .1, .2, .4, .8 mg/kg as the base in saline particle) administered only once per week if the following criteria were met. A given day served as a baseline control day (day 1) if the response rate for that day was within the range of rates obtained over the immediately preceeding 5-10 days of stable responding. Saline was administered on the next day (day 2). If responding after saline remained within the range of previous stable responding, (-)-nicotine was administered on the following day (day 3). This sequence occurred once per week with the remaining two days serving as baseline sessions. Injections were administered s.c. in a volume of 1 ml/kg of body weight. (-)-Nicotine doses were administered in an ascending order. A complete dose-effect function was determined for each rat and then repeated. (-)-Nicotine effects were expressed as a percentage of the mean of the preceeding baseline and saline data. These percentages were averaged to give mean saline and (-)-nicotine effects for each rat, which were then averaged across animals to yield group functions.

Four weeks after the completion of the acute (-)-nicotine dose-effect determinations the chronic dosing phase was begun. The rats were divided into two groups (N=7 per group) and watched for overall session response rat. Saline was injected twice per day for five consecutive sessions, with the mean of these five sessions serving as control data for the chronic dosing phase. For the next 30 consecutive days, one group of rats (the before group) received .8 mg/kg of (-)-nicotine before and saline after the session. The other group

of rats (the after group) received saline before and .8 mg/kg of (-)-nicotine after the session. Injections occurred 10 minutes before and after the session. On day 31 of chronic nicotine dosing the after group received the .8 mg/kg dose of (-)-nicotine before the session as a test for tolerance; saline was administered after the session. The before group received its usual pre-session (-)-nicotine and post-session saline injections on day 31. Following day 31 the before and after groups continued to receive their usual pre- and post-session (-)-nicotine or saline injections except that testing occurred only on Monday through Friday. On weekends the rats from both groups received a single injection of .8 mg/kg of (-)-nicotine. Beginning on day 52 of chronic (-)-nicotine dosing the acute (-)-nicotine dose-effect functions were redetermined. One day per week (Thursdays or Fridays) a test dose of (-)-nicotine was substituted for the usual presession injection, .8 mg/kg (-)-nicotine or saline, in both the before and after groups; saline was administered post-session to both groups. The substitute doses of (-)-nicotine were .2, .4, .8, 1.2 and 1.6 mg/kg administered in an ascending order. Additionally, both groups of rats received saline presession as the substitute dose and .8 mg/kg of (-)-nicotine post-session the week before (day 45) and the week after the acute (-)-nicotine dose-effect function was redetermined. Chronic (-)-nicotine dosing was terminated after approximately 100 consecutive days. All rats received their last dose of chronic (-)-nicotine on a Friday. Following termination of chronic (-)-nicotine dosing the persistence of tolerance was examined over the next four weeks. Animals were tested Monday through Friday with Wednesdays serving as baseline sessions, Thursdays serving as saline control sessions, and Fridays serving as (-)-nicotine test sessions. On Fridays .8 mg/kg of (-)-nicotine was administered presession to all rats.

Data Analysis

Performance measures included overall session response rates and the time to complete the first FR. Response frequencies were also collected in five successive six minute bins to examine the within-session time course of (-)-nicotine's action.

RESULTS

All rats had characteristic FR rates and patterns of responding (Ferster and Skinner, 1957). Food pellet delivery was followed by a short pause in lever pressing and then by a high response rate that was sustained until the ratio was completed and the next reinforcer was delivered.

Figure 1 shows the initial dose-effect functions for the effects of (-)-nicotine on response rates (filled circles). The overall session baseline response rates (mean ± SE) were 2.43 ± 0.30 responses/sec for the before group and 2.39 ± 0.24 responses/sec for the after group. Nicotine produced small decreases in overall response rates at the lower doses (.05, .1 and .2 mg/kg) and more pronounced dose-dependent decreases at the .4 and .8 mg/kg doses (Figure 1, top). The dose effect functions for the before and after groups were similar.

The typical pattern in the cumulative records following nicotine administration was a suppression of lever pressing early in the session followed by recovery of control-like rates after the completion of several ratios. Occasionally, rates of responding following recovery exceeded control rates. The time of maximal rate reduction, therefore, occurred during the first six minute segment of the session. Response rates during minutes 0-6 were reduced in a dose-dependent manner and to a similar degree in both groups of rats (Figure 1, botton, filled circles). Rates were decreased by 50 - 60% by .4 mg/kg of (-)-nicotine and were almost totally suppressed by .8 mg/kg.

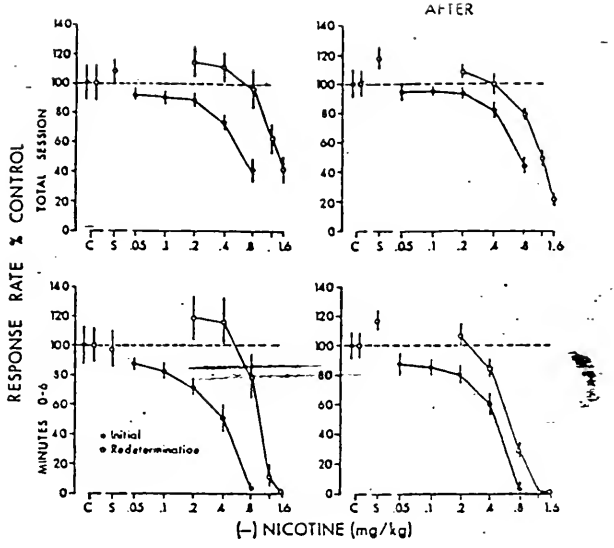


Figure 1. Effects of nicotine on FR 32 response rates during the total 30 minute session (top) and during the first six minutes of the session (bottom). The initial dose-effect functions were determined before chronic nicotine dosing. The redetermined dose-effect functions were determined beginning after 45 days of chronic nicotine dosing. The before group (left side) received nicotine chronically before the session. The after group (right side) received nicotine chronically after the session. Each point represents the mean of seven rats; vertical lines indicate 1 S.E.. Points above C represent control responding; the mean is indicated by 100% on the ordinate. Points above S indicate saline administered twice presession as part of the redetermined dose-effect functions.

Overall session response rates averaged for the five saline control sessions preceeding chronic (-)-nicotine administration were 2.62 ± 0.29 and 2.59 ± 0.23 response/sec for the before and after groups, respectively. These control rates were similar to the control rates occurring previously during acute nicotine dosing ~~(see above).~~ On day 1 of chronic dosing with .8 mg/kg of (-)-nicotine, the overall session response rate for the before group was reduced to 48.6 ± 9.3% of its mean control level (Figure 2, top). This reduction was not significantly different from the reduction to 40.9 ± 7.1% of control found with the same dose of (-)-nicotine previously administered acutely. Daily dosing with .8 mg/kg of (-)-nicotine resulted in a gradual attenuation of the reduction in response rate over the first 10 days (i.e., tolerance). From day 10 to day 30 overall response rates were reduced to 80-90% of mean control levels. For the group receiving (-)-nicotine after the session, overall response rates did not differ from control values over the first 30 days of chronic dosing. On day 31 both groups received .8 mg/kg of nicotine before and saline after the session. Response rates were reduced by nicotine on day 31 to a significantly greater degree in the after group than in the before group (Student's t-test, $p<.05$). In the before and after groups, respectively, response rates were reduced to 90.6 ± 9.8% and 62.6 ± 7.4% of control values on day 31. The reduction in response rate in the before group was significantly less than the reduction observed in the after group ($p<.05$), suggesting that the before group was more tolerant than the after group to nicotine.

To determine whether tolerance had also developed to some degree in the after group, the effects of (-)-nicotine on day 31 were compared to those obtained during the initial dose-effect determination. The initial reduction in overall response rates to 40.9 ± 5.0% of control was significantly greater

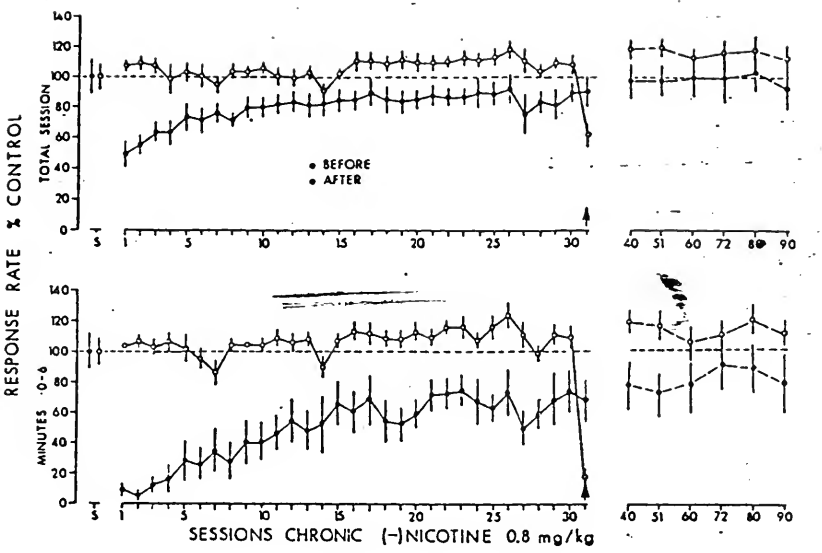


Figure 2. Effects of daily administration of 0.8 mg/kg of nicotine on FR 32 response rates during the total 30 minute session (top) and during the first six minutes of the session (bottom). The before group received nicotine before and saline after the session; the after group received saline before and nicotine after the session. On day 31 both groups received nicotine before and saline after the session. Each point is based upon the data from seven rats; vertical lines indicate 1 S.E.. Points above S represent saline control responding; the mean is indicated by 100% on the ordinate. Saline control points are the mean of five consecutive saline sessions which immediately preceeded chronic nicotine administration.

than that found on day 31 of chronic dosing ($p<.05$). This indicates that some tolerance to (-)-nicotine also developed with postsession administration.

In the before group, response rates during the first six minutes of the session on day 1 of chronic dosing were markedly suppressed to 7.7 ± 4.8% of control levels. This was similar to the response rate reduction to 3.6 ± 2.6% of control found with .8 mg/kg of (-)-nicotine administered ~~acutely~~ initially. Mean rates of responding increased gradually across sessions of chronic dosing and were relatively stable from sessions 21 to 30 at 60% to 74% of control. Responding in the after group was unaffected by the postsession administration of nicotine except for several sessions in which rates were slightly decreased (days 7 and 9) or increased (day 26). On day 31, presession administration of nicotine reduced response rates during minutes 0-6 of the session in the before group to 68.1 ± 13.7% and in the after group to 17.7 ± 4.7% of control values; this difference was statistically significant ($p<.05$). Nicotine produced slightly though significantly ($p<.05$) smaller decrease in response rates in the after group on day 31 than it did initially before chronic dosing; response rates were reduced initially to 3.2 ± 1.7% of control levels (Figure 1).

For approximately 70 additional days the before/after dosing regimen was continued. Over this period the overall response rate of both groups increased slightly and stabilized such that the before group's mean rate was at about 100% and the after group's mean rate was at about 120% of control levels (Figure 2, top). Responding during the first six minutes of the session in the before group continued to be suppressed throughout chronic dosing with the average nicotine rate at about 80% of the mean control rate.

The nicotine dose-effect functions determined during chronic dosing are presented in Figure 1 (open circles). Compared to the initial dose-effect functions, response rates in both groups of rats were decreased less by all

doses of nicotine after chronic dosing. Attenuated rate decreases were greater in the before group than in the after group; their difference was most pronounced at the .8 mg/kg dose for rates during minutes 0-6 of the session. Two additional higher doses of nicotine (1.2 and 1.6 mg/kg) decreased overall response rates to a lesser degree in the before group than in the after group. In the before group, 1.6 mg/kg reduced overall response rates to a similar degree as .8 mg/kg initially. In the after group, 1.2 mg/kg reduced overall response rates to a similar degree as .8 mg/kg initially, and 1.6 mg/kg reduced response rates to a greater degree. Redetermination of the effects of the lower doses of nicotine (.2 and .4 mg/kg) revealed that response rates were now increased beyond control levels to a small degree in the before group but not in the after group following chronic dosing. Substituting saline for the usual presession administration of .8 mg/kg of nicotine in the before group produced no observable changes in response rates. These results indicate that there was a greater shift to the right in the dose-effect functions of the before group than of the after group, further suggesting that the development of tolerance to nicotine was enhanced by presession administration.

Nicotine increased the latency to complete the first ratio as a function of dose in both groups of rats (Table 1). Tolerance developed with chronic dosing in the before group such that the latency to complete the first ratio gradually decreased over sessions 1 to 30; latencies were still somewhat lengthened compared to control on day 30 (Table 1). Chronic nicotine did not alter latencies in the after group over sessions 1 to 30. On day 31 the presession administration of .8 mg/kg of nicotine produced a markedly longer latency in the after group than in the before group; due to intersubject variability this difference just failed to achieve statistical significance ($p > .05$). Redetermination of the dose-effect functions revealed shorter

Table 1

Nicotine dose-effect functions for latency in seconds to complete the first fixed-ratio (Mean ± SE)

				NICOTINE DOSE (mg/kg)						
GROUP	DOSE-EFFECT	CONTROL[a]	SALINE[b]	0.05	0.1	0.2	0.4	0.8	1.2	1.6
BEFORE	INITIAL	14 ± 2	---	23 ± 6	32 ± 8	33 ± 6	100 ± 19	637 ± 79	---	---
	REDETERMINED	19 ± 2	66 ± 17	---	---	27 ± 6	24 ± 9	37 ± 12	396 ± 94	674 ± 68
AFTER	INITIAL	17 ± 7	---	54 ± 34	24 ± 7	28 ± 6	69 ± 14	572 ± 54	---	---
	REDETERMINED	24 ± 3	18 ± 2	---	---	26 ± 5	32 ± 6	152 ± 43	646 ± 77	1005 ± 102

[a] Initial dose-effect: mean of baseline and saline sessions immediately preceeding nicotine administration were averaged across 10 nicotine administrations (each of 5 doses administered twice). Redetermined dose-effect: mean of five consecutive saline sessions immediately preceeding chronic nicotine administration.

[b] Saline administered twice presession as part of the redetermined dose-effect function.

Table 2

Latencies in seconds (Mean ± SE) to complete the first fixed-ratio over the first 31 sessions of chronic nicotine (.8 mg/kg) administration

		SESSION							
GROUP	SALINE[a]	1	5	10	15	20	25	30	31[b]
BEFORE	19 ± 2	571 ± 126	230 ± 58	141 ± 42	51 ± 19	81 ± 26	74 ± 26	54 ± 24	57 ± 20
AFTER	24 ± 3	24 ± 6	20 ± 4	31 ± 10	32 ± 16	27 ± 6	17 ± 3	32 ± 6	294 ± 111

[a] Mean of five consecutive saline sessions immediately preceeding chronic nicotine administration.

[b] Nicotine administered presession to both groups of rats.

latencies than observed initially in both groups at all doses tested (Table 1). At .2 -.8 mg/kg the redetermined latencies of the before group were not different from control, while at .8 mg/kg the latency of the after group was substantially lengthened compared to its control. Further, the two groups differed significantly from each other at .8 mg/kg ($p<.05$). The 1.2 and 1.6 mg/kg doses increased latencies in both groups with greater increases observed in the after group.

The persistence of tolerance as determined by weekly administrations of .8 mg/kg of nicotine following the cessation of chronic dosing is shown in Figure 3. Response rates in the before group were reduced less than in the after group by nicotine during weeks 1 and 2. By week 3 response rates were reduced to a similar degree in the two groups by nicotine. Since both groups exhibited a small loss of tolerance each week over weeks 1 to 3, it was necessary for the before group to show a greater loss of tolerance than the after group in order for both groups to respond similarly to nicotine during week 3. Response rates were similarly or slightly less affected by nicotine delivery during week 4 compared to week 3, suggesting that a stable level of responding had been achieved with weekly nicotine administrations. Response rates were reduced less by .8 mg/kg of nicotine during weeks 3 and 4 than during the initial dose-effect determinations (filled circles), suggesting that some degree of tolerance persisted in each group.

Following cessation of chronic dosing, latencies to complete the first ratio in the before group were lengthened less by nicotine than were latencies in the after group over all four weeks (Table 3); group differences were significant for weeks 1 and 2 ($p<.05$). Latencies increased in each group over weeks 1 to 3, although only the before group showed significant increases from

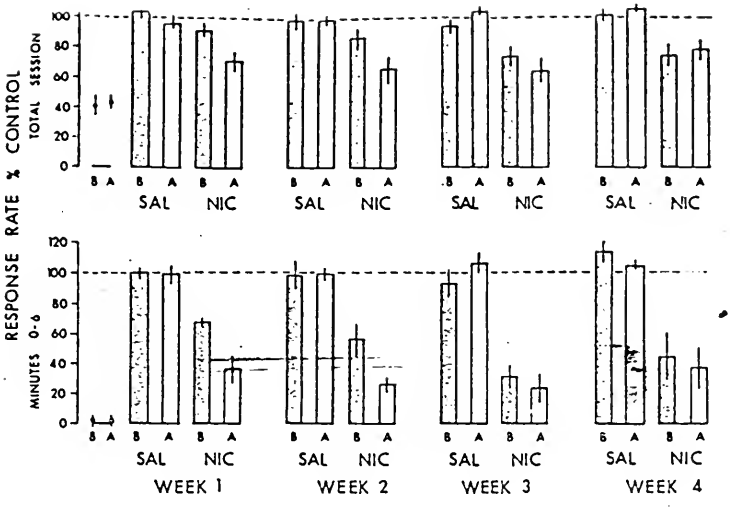


Figure 3. Persistence of tolerance to the effects of 0.8 mg/kg of nicotine on FR 32 response rates following cessation of chronic dosing. Response rates are from the total 30 minute session (top) and from the first six minutes of the session (bottom). The before group (B) had received nicotine chronically before the session; the after group (A) had received nicotine chronically after the session. The weekly testing sequence was baseline (Wednesday), saline (Thursday) and nicotine (Friday). Data are as percentage of respective control mean, indicated by 100% on the ordinate. Control for the saline (SAL) was the preceeding baseline session. Control for nicotine (NIC) was the mean of the preceeding baseline and saline sessions. The points to the left indicate the initial acute effects of 0.8 mg/kg of nicotine. Vertical lines indicate 1 S.E.

Table 3

Effects of .8 mg/kg of nicotine on latency (Mean ± SE) to complete the first fixed-ratio when administered once per week following the cessation of chronic nicotine.

	BEFORE		
Nicotine Administration	Baseline	Saline	Nicotine
Initial	16 ± 2	13 ± 2	637 ± 79
Week 1	19 ± 6	13 ± 2	29 ± 15
Week 2	14 ± 5	10 ± 1	49 ± 19
Week 3	16 ± 5	14 ± 5	161 ± 65
Week 4	25 ± 10	17 ± 4	95 ± 27

	AFTER		
Nicotine Administration	Baseline	Saline	Nicotine
Initial	18 ± 2	17 ± 2	572 ± 54
Week 1	15 ± 3	16 ± 2	150 ± 58
Week 2	18 ± 2	16 ± 3	194 ± 62
Week 3	16 ± 2	19 ± 7	254 ± 77
Week 4	18 ± 4	16 ± 3	171 ± 64

week to week. Nicotine-induced increases remained shorter than those observed during the initial dose-effect determinations.

DISCUSSION

The present results confirm the findings of previous studies which demonstrated that tolerance develops to the behavioral effects of nicotine following chronic administration (e.g., Morrison and Stephenson, 1972; Stolerman et al., 1974; Jones et al., 1978), including tolerance to the disruption of FR responding (Domino and Lutz, 1973; Dougherty et al., 1981; Hendry and Rosecrans, 1982). These results extended previous findings by demonstrating that once tolerance develops to a given dose of nicotine, higher doses are required to produce effects quantitatively and qualitatively similar to those observed before tolerance developed. Thus, nicotine tolerance was seen here as a shift to the right in the dose-effect functions for measures of response rate reduction and increases in latency to complete the first ratio. There is general agreement that tolerance is defined as a lessened effect of a given dose of a compound following its repeated administration and by the recoverability of the initial effects by administering higher doses (Krasnegor, 1978). Shifts to the right in complete dose-effect functions have not been reported previously in studies of nicotine tolerance. The alterations in the effects of nicotine following chronic administration reported here satisfy both criteria for identifying tolerance.

The major finding of the present study was that the development of tolerance to nicotine was highly dependent on factors arising from the nicotine-induced disruption of FR responding, rather than on the mere repeated administration of nicotine. Thus, behavioral factors appear to be critically involved in the mechanism(s) underlying nicotine tolerance. This is evidenced by the

finding that the before group was more tolerant than the after group when comparisons were made after 30 days of dosing, and by the greater shift to the right in the nicotine dose-effect functions of the before group than the after group when these functions were redetermined during chronic dosing.

The tolerance reported here was not only dependent on behavioral factors stemming from nicotine-induced disruption of FR responding, however, since the after group also showed some tolerance. This finding suggests that the development of tolerance to nicotine under the conditions used here involves two components. One component evident only in the before group involves a behavioral adaptation of the organism to the disruptive effects of nicotine on schedule-controlled responding. This is consistent with the reinforcement density hypothesis which states that tolerance to the behavioral effecs of a compound is more likely to occur when the compound interferes with an organism's ability to satisfy the requirements for reinforcement; that is, when exposure to the compound results in a loss of reinforcement (Schuster et al., 1966; see Corfield-Sumner and Stolerman, 1978 for a review). The other component of tolerance more directly implicates certain adaptation mechanisms resulting from the repeated exposure to nicotine; these mechanisms would be expected to operate in both the before and after groups. These mechanisms are typically thought of as alterations in distribution and/or receptor sensitivity (Levine, 1978). It is presently unclear how behavioral, dispositional and receptor sensitivity factors interact in situations where behavioral tolerance occurs.

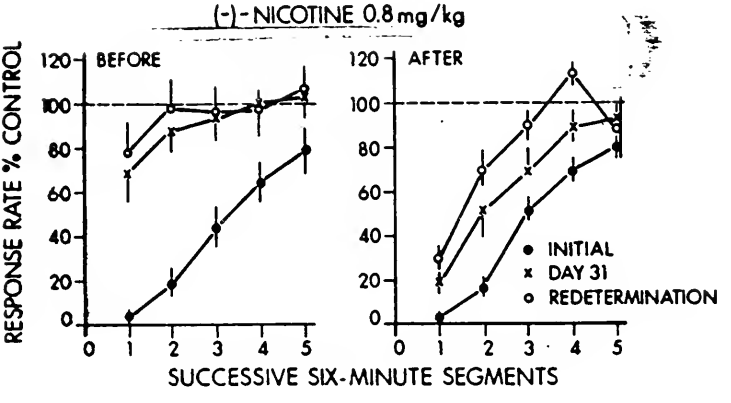
In contrast to the present results, Hendry and Rosecrans (1982) concluded that behavioral variables do not influence the development of tolerance to nicotine. In their study, male mice responded under a FR 25 schedule of sweetened milk reinforcement. Tolerance to the rate-decreasing effect of 1.2 mg/kg of nicotine (free base) developed in the before group after 30 days of

dosing. Redetermination of the nicotine dose-effect function (.2 - 1.6 mg/kg) while daily dosing continued showed that the before and after groups were affected similarly at all doses. Following cessation of chronic dosing, both groups lost tolerance at similar rates. Since factors such as age, gender and strain have been shown to influence the behavioral effects of nicotine in both rats and mice (Bryson et al., 1981; Hatchel and Collins, 1977; Morrison, 1968), and since the mouse has only recently been used in behavioral pharmacological studies involving schedules of inforcement, critical comparisons between this study and this present one cannot be made at the present time.

Nicotine administered acutely decreased food-maintained FR 32 response rates in a dose-dependent fashion. The reduction in total session responding was due to a complete suppression of responding early in the session followed by a rapid recovery of control-like rates. Similar effects of nicotine on FR schedules have been reported previously in rats (Pradham, 1970; Domino and Lutz, 1973; Dougherty et al., 1981), mice (Hendry and Rosecrans, 1982) and squirrel monkeys (Davis et al., 1973; Spealman et al., 1981). In contrast, Marrison (1967) reported that at doses similar to those used in the present study (.05 - .4 mg/kg), total session response rates were increased in rats responding under an FR 30 water reinforcement schedule. In Morrison's study, however, the daily session was 90 minutes in duration; the session pattern of responding consisted of an initial reduction in responding followed by large rate increases after 60 minutes had elapsed. In the present study, small increases in rates were observed in some subjects following recovery of responding after nicotine administration. More consistent rate increases may not have been observed here because test sessions were 30 minutes in duration. Pradham (1970) also has reported that nicotine increased FR rates during 60 minutes test sessions. FR and continuous avoidance components alternated with-

Since nicotine increased FR response rates only when

in a multiple schedule, and not when FR occurred alone or as part of a multiple fixed-interval fixed-ratio schedule, the nicotine-induced rate increases were most likely due to an interaction between the water and shock conditions maintaining response.



Mr. WYDEN. Now, you have indicated that your work showed that rats did develop the tolerance to nicotine. You have indicated that this is one of the warning signals of potential abuse liability or addiction. I'm curious, my understanding is that you submitted this particular manuscript that I cited, to the management of Philip Morris. You were seeking approval to publish the results.

When you asked them for approval to publish those results—results that to me seem important for the public—were you denied the right to publish them?

Mr. DENOBLE. Yes. Let me just say two things about that work first. We were certainly not the first to demonstrate nicotine tolerance, that has been shown for a long time. This study identified certain behavioral parameters that contributed to nicotine tolerance.

So after conducting this study and asking to get it out, and submitting it, we thought it was a relatively benign study because, although tolerance is a characteristic of many drugs of abuse, it is not necessarily a predictor of abuse, but it is a characteristic of many compounds. We thought it was relatively benign.

The company saw it as very threatening because the word "tolerance" was appearing at that time in the Diagnostic and Statistical Manual of the American Psychiatric Association as a criterion or an indicator of drug dependence. By using that criterion, they felt this work was too dangerous and one, would not let it go out, and two, did not want further tolerance work to continue.

Mr. WYDEN. So, in effect, what you are saying is because you were showing that these studies were showing a tolerance for nicotine, this would establish a drug dependence, and this was again defined by a major health group, the American Psychiatric Association, and this would be damaging to them?

Mr. MELE. Well, let me clarify. I think Philip Morris' assessment of the work was wrong. I don't think tolerance, again, identifies necessarily dependence-producing agents. It is a characteristic of many of those but it is not a single identifying characteristic. But they misidentified the DSM manual and made their judgment.

Mr. WYDEN. In addition to saying that you couldn't publish the tolerance paper, did the management there take other steps to curtail your research into tolerance?

Mr. MELE. Well, they preferred that tolerance work did not continue.

Mr. WYDEN. So you were——

Mr. WAXMAN. If the gentlemen would yield. Let's just get names, if we could, for the record. Who are these people you are talking about?

Mr. MELE. Dr. Jim Charles was the one who came to my office with the manuscript review request and asked me to write an internal document, but that it could not go out because it demonstrated tolerance. And in his mind, or somebody's mind, it indicated a dependence-producing situation.

Mr. WYDEN. In terms of what happened after they said you couldn't publish the paper, did you communicate to the management, Mr. Charles specifically, that you wanted to examine whether rats develop tolerance that would cause them to suffer physical

withdrawal symptoms? And then the management said, you are not allowed to do this work?

Mr. MELE. Not specifically in that way. Our plan was with these data to pursue the role of tolerance and other aspects of nicotine use. To see how tolerance would influence self-administration, to see how tolerance would influence physical dependence. We weren't able to pursue those studies as a result of this study.

Mr. WYDEN. But the management said that you could not pursue that additional work?

Mr. MELE. I don't recall specifically talking to them about those specific studies, but just tolerance in general was something—was not something they wanted pursued.

Mr. WYDEN. Dr. Mele, do you know Dr. Kathy Ellis?

Mr. MELE. Yes.

Mr. WYDEN. Now, Dr. Ellis testified about the tolerance issue at the hearing on April 14th, when she appeared with the CEO of Philip Morris, Mr. Campbell. Now, let me read you what she said to our subcommittee then.

She said, and I quote, "The strict pharmacological definition of addiction involves three different criteria: they are intoxication, physical dependence, and tolerance. And to my knowledge, there is no evidence that nicotine or cigarette smoking plays in any of these definitions." So it seems to me what Dr. Ellis did was, in effect, deny the very work that you did at Philip Morris.

Mr. MELE. I don't know what access she had back then to our work. I would assume currently, in her current position, she would have been aware of it. So, yes, she was not recognizing that, nor recognizing a large body of literature on nicotine tolerance.

Mr. WYDEN. And she was a colleague of yours at the Richmond research center, isn't that correct?

Mr. MELE. Correct.

Mr. WYDEN. Mr. Chairman, again, I think what we have here is another example of a serious misstatement by the Philip Morris Company, contrary to the findings of Dr. Mele's report. Dr. Mele, of course, has indicated that he was a colleague of Dr. Ellis' at the Richmond research center.

What Dr. Ellis said to the subcommittee is that Philip Morris has no evidence that nicotine causes tolerance. So I would hope that before too long we ask for further information on this matter, because it appears to me to be yet another serious misstatement by Philip Morris.

Mr. MELE. Congressman, I would just like to add, and clarify that. Kathy Ellis did not work in our laboratory, she had her own laboratory, but we were part of the same division.

Mr. WYDEN. Mr. Chairman, I yield back.

Mr. WAXMAN. Would she have had access to your work?

Mr. MELE. In the beginning, I don't know. I don't think so because it was kept very secret. Although at one point, once we were allowed to present our data to the division and to the rest of the research center, she would have been familiar with it.

Mr. WAXMAN. OK. Thank you.

Mr. WYDEN. Mr. Chairman, I yield back.

Mr. WAXMAN. Thank you, Mr. Wyden. Mr. Kreidler?

Mr. KREIDLER. Thank you, Mr. Chairman. You have said that the purpose of the analogue program was to develop a nicotine analogue that had the brain effects of nicotine, but not the heart effects, if I recall correctly. Was the initial idea, as far as you understand, to develop a safer cigarette?

Mr. DENOBLE. That's correct, yes.

Mr. KREIDLER. Where were the analogues developed?

Mr. DENOBLE. They were synthesized at the Richmond center, the organic laboratory.

Mr. KREIDLER. And do you know who headed that clinical group?

Mr. DENOBLE. Dr. Jeff Seaman headed the group. Chuck Shevdarian was also another chemist in the group.

Mr. KREIDLER. They were at Philip Morris then?

Mr. DENOBLE. They were back in 1984. I don't know where they are now.

Mr. KREIDLER. OK. It is my understanding that part of the analogue testing was done in Rochester and part in Richmond. Could you tell us what the relationship between the work in Rochester and the work in Richmond was?

Mr. DENOBLE. Yes. The analogues would be synthesized in Richmond, Va., and they would first be sent to Rochester, Dr. Leo Abood's laboratory. What Leo would do would be screen the analogues in a receptor binding assay, to see whether the analogue recognized the nicotinic receptor, you know, in brain. He was using torpedo fish membranes, but it's the same thing.

At that point we would determine whether or not it had the same—whether the receptor said, gee, you look like nicotine. We would then get some data on whether or not it produced contractions in guinea pig ilium, which would be a predictor of cardiac activity.

At that point, that data would be sent back down to us in our laboratory, and we would screen the compound. If it was good data, if it met the criteria of good data, we would screen the compound in our tests in animal behavior to determine whether it looked like nicotine.

Mr. KREIDLER. So it was, at least, the tobacco version of nicotine that was causing the cardiovascular type of reaction then, as far as you could determine?

Mr. DENOBLE. I'm not sure I understand the question.

Mr. KREIDLER. The cardiovascular responses of nicotine were associated with the tobacco form, and there were perhaps some other forms of nicotine——

Mr. DENOBLE. There is a couple of different forms of nicotine, but the presser effect you get is with the L-form of nicotine, yes.

Mr. KREIDLER. I see. I would like to distribute Exhibit 18-A, which was part of the 1980 memorandum explaining the work of the nicotine receptor program in Rochester, Mr. Chairman, if that is all right?

Mr. WAXMAN. Without objection, that will be submitted for the record, and identified as the next exhibit in sequential number.

[Exhibit 18A follows:]

PHILIP MORRIS U. S. A.

INTER-OFFICE CORRESPONDENCE

RICHMOND, VIRGINIA

Abood 18A

CONFIDENTIAL

To: Dr. R. B. Seligman Date: March 18, 1980

From: J. L. Charles

Subject: Nicotine Receptor Program - University of Rochester

Nicotine is a powerful pharmacological agent with multiple sites of action and may be the most important component of cigarette smoke. Nicotine and an understanding of its properties are important to the continued well being of our cigarette business since this alkaloid has been cited often as "the reason for smoking" and theories have been advanced for "nicotine titration" by the smoker. Nicotine is known to have effects on the central and peripheral nervous system as well as influencing memory, learning, pain perception response to stress and level of arousal.

It is not suprising that a compound with such a multitude of effects would have properties which are considered undesirable by the anti-smoking forces. Claims are made that nicotine in cigarette smoke can induce chest pain and irregularities in cardiac rhythm when a person with a compromis cardiovascular system smokes or when persons with cardiac disease are exposed to high concentrations of side stream smoke

For these reasons our ability to ascertain the structural features of the nicotine molecule which are responsible for its various pharmacological properties can lead to the design of compounds with enhanced desirable properties (central nervous system effects) and minimized suspect properties (peripheral nervous system effects). There are many opportunit for acquiring proprietary compounds which can serve as a firm foundation for new and innovative products in the future.

The above is an excerpt from an introduction to the nicoti program which I wrote on 12/1/78. My views have not significan changed since that time. I believe that nicotine does plsy an important role in the smoking process. How important that role is remains to be determined. The receptor program at the University of Rochester is an integral part of the nicotine program and can be justified in a number of ways. An initial thought was that Dr. Abood would have the knowledge and techniq to perform screening of nicotine analogs for CNS activity. The synthesis group has created a number of interesting compoun which are now being screened by Dr. Abood. In addition Dr. Abood was to carry out fundamental studies on sites and mechanisms of action of nicotine in the brain. That research is in progress.

PLAINTIFF'S EXHIBIT 5224

1003289974

I sat in on an additional meeting with Dr. Abood and Drs. Sanders, Seeman, and Chavdarian during Dr. Abood's last visit. I found the discussions to be useful and felt that Dr. Abood was doing some very interesting work which can ultimately be of benefit to Philip Morris. I also utilized Dr. Abood as a consultant during that visit and he made some good suggestions and I thought the time was well spent.

In summary, the nicotine receptor program at the University of Rochester is an integral part of our overall nicotine program. The combination of basic research on the pharmacology of the nicotine receptor combined with the capability to screen nicotine analogs for CNS activity complements our internal synthetic and behavioral efforts in the nicotine program. The program is justified in my view as a defensive response to the anti-smoking forces criticisms of nicotine and also as fundamental research into the nature of our product and how it affects our customers, the smokers. This entire program involves complex technological problems and the benefits to be derived from the program will not be realized immediately. Indeed the benefits will necessarily be of a long-term nature and may have direct bearing on our market position in a 10-15 year time frame. However, if we do not have the basic research results this program will provide we will not be in a position to respond if and when the pressures to change do occur.

JLC/mro
cc: Dr. T. S. Osdene

Mr. KREIDLER. I find the first sentence of the memo particularly interesting. It states, "Nicotine is a powerful pharmacological agent with multiple sites of action and may be the most important component in cigarette smoke." This certainly paints a different picture of nicotine than the picture painted by the tobacco company executives 2 weeks ago. Do you have a response to that?

Mr. DENOBLE. This statement, that it is a powerful pharmacological agent, justified much of the research at the research center. I mean, the whole thrust of research of this program was work on nicotine not as a flavorant but as a pharmacological agent.

It was our belief back then and my belief today that nicotine is an agent in cigarette smoke that is reinforcing, and it is a contributor to why people smoke. That was the premise of our whole program.

Mr. KREIDLER. Now I would like to show Exhibits 19, 20, and 21, which are the pictures of rats in the analogue program.

Mr. KREIDLER. Doctor, would you please tell us what we're seeing in these pictures here?

Mr. DENOBLE. The poster on, I guess, my right, is a picture of an animal who has been anesthetized. And we are placing a canula, basically a needle, into different areas of its brain.

The work that came out of Leo Abood's lab in Rochester indicated that if you placed nicotine directly in the brain, that the animal would have a particular behavioral response. And he went on to show, very elegantly, that effect was only produced with nicotine-like drugs.

So we went back to our lab, cannulated animals to see if we could replicate and extend his findings and use it as a tool. The center picture is an animal who is reaching up to grab a pellet of food. He's got a brain canula, and we injected 5 microliters of nicotine into his brain, and that's the same animal in the last photograph.

You can see he is not responding to the food pellet. That syndrome was called prostration syndrome. It was unique to nicotine. The animal becomes splayed, he becomes unresponsive for about 12 minutes. We went on to characterize that behaviorally, to show pharmacologically that it was an effect of nicotine on brain receptors. And that was a primary screening tool in our laboratory in the nicotine analogue program.

Mr. KREIDLER. Did you succeed in developing a nicotine analogue that would have the effects that nicotine has on the brain but does not have nicotine's effect on the heart?

Mr. DENOBLE. We did identify a series of analogues that met our minimal criteria for that effect, yes.

Mr. KREIDLER. Did Philip Morris ever use the analogues, to the best of your knowledge?

Mr. DENOBLE. No, sir. I have no knowledge of that.

Mr. KREIDLER. Do you know why not?

Mr. DENOBLE. No. We had several discussions about what we would do with it when we found it. And once we found it, nothing was done with it. The indications to us were that we'll take a wait-and-see attitude.

Quite honestly, I think that scientifically that was an interesting finding. It could be conceived of as a major breakthrough, in my

mind, to disassociate brain effects from peripheral effects. But they never chose to follow that to the next logical scientific conclusion.

Mr. KREIDLER. Do you have any suspicions that level of research might be something they couldn't keep control of at some point in the future, that might have influenced whether they wanted to follow up on these analogues?

Mr. DENOBLE. No, I don't believe that. I think that the research facility was quite capable of following up on those analogues and doing a lot more work. And, quite frankly, sir, it may have been done. I am just not aware of it.

Mr. KREIDLER. I see. Smoking causes over 150,000 deaths each year from heart disease. Your work at Philip Morris shows that there might be a replacement for nicotine in cigarettes that would duplicate the brain's effects of nicotine but would not have nicotine's effect on the heart.

Yet, after you succeeded in developing an analogue, Philip Morris' response was to put your discovery on the shelf. Presuming that no follow-up was done, does that trouble you?

Mr. DENOBLE. Well, sure. I mean, it troubles me a lot. To the best of my knowledge it was put on the shelf. It may not have been put on the shelf.

Also, recognize that there is a large leap from our laboratory, from Rochester data, from in-house data, and going into a product. I mean, this analogue would have to go through many, many, many other tests. And I think from a scientific point of view, it was disturbing that they didn't choose to do those other tests. At least, we have no knowledge that they did.

Mr. WYDEN. Will the gentleman yield?

Mr. KREIDLER. I yield.

Mr. WYDEN. I thank my colleague. Let me just be real brief. Wouldn't it have been in the public interest right at that point to aggressively have pursued this new research? I mean, here we have a situation, my colleague has basically said that the evidence looks to us like it was put on the shelf, a situation where smoking causes 150,000 deaths as a result of heart disease.

My colleague has pointed out, you know, here is an opportunity to really do something to help people. Wouldn't it have been in the public interest to have aggressively done the research right at that point, so that you and other scientists would be able to tell us today what you know about it?

Mr. DENOBLE. Yes, sir, absolutely.

Mr. WYDEN. I thank my colleague for yielding.

Mr. WAXMAN. Will you also yield?

Mr. WYDEN. Certainly.

Mr. WAXMAN. I thought one of the ideas of scientific inquiry was that you go as far as you can go and then other scientists can pick up from where you left off. But if this information is never made public, or never given to other scientists, there is no way that some of these advances can be pursued.

And I'm hoping that we can follow up further this trail because this is a new revelation that perhaps cigarettes maybe could have been made healthy, but at least could have been made in a way that would have avoided the deaths from the heart problems that came from the nicotine.

We've always heard about nicotine as an addicting substance, but now we're learning nicotine is a problem that affects the heart as well. Could you give us the name of the compound that might have been a successful analogue?

Mr. DENOBLE. I'm not a chemist, but I can give you—it was called two-prime methalnicotine.

Mr. WAXMAN. Thank you very much. Mr. Kreidler, did you want to pursue further questions?

Mr. KREIDLER. I think my time has expired. Thank you very much, Mr. Chairman.

Mr. WAXMAN. Dr. DeNoble, did you look for other substances in tobacco or tobacco smoke that have effects on the brain?

Mr. DENOBLE. Yes, we did. In late 1981, early 1982, we raised the question of whether or not there could be other things in cigarette smoke that may have biological activity.

Mr. WAXMAN. And what did you look at?

Mr. DENOBLE. What we did was we did basically a computer search of the components that are identified in cigarette smoke. And we looked through the list and we found—a compound that stuck out in our mind was acetaldehyde. This is a compound that has a reasonably high concentration in cigarette smoke; it's a highly volatile compound.

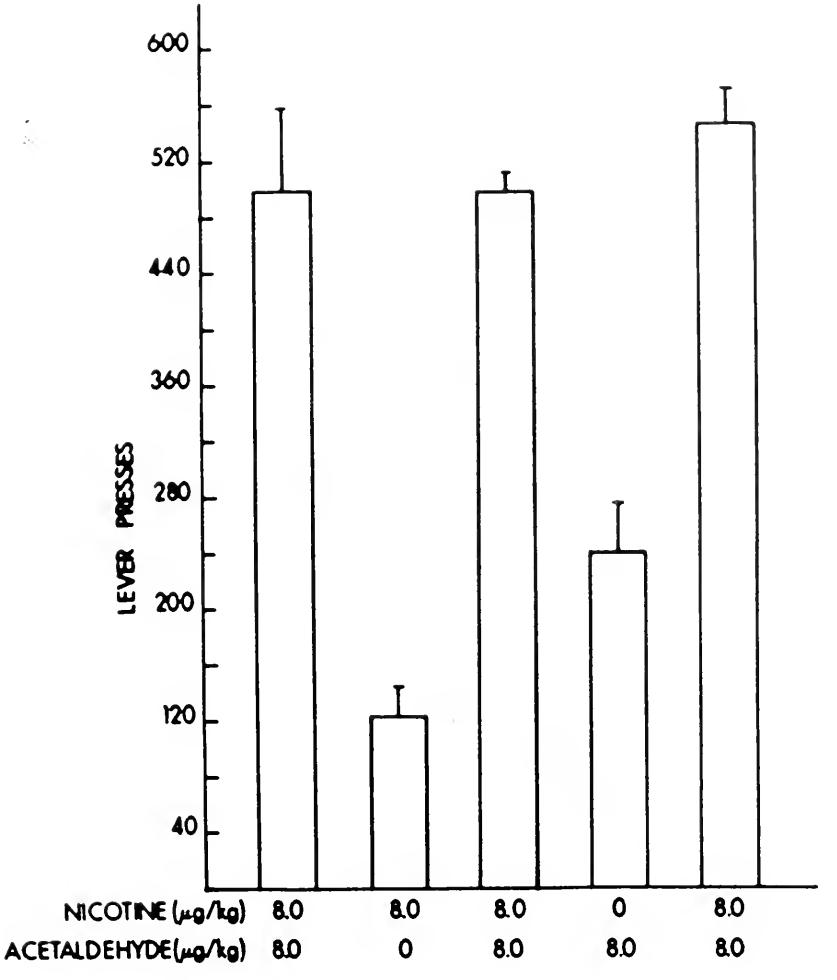
And it was really kind of serendipitous because the work—you really wouldn't think this is anything hot, but I had just come off of doing post-doc where I recognized that acetaldehyde is a major metabolite of alcohol. And there were some theories in the 1970's that this metabolite would react in the brain with other chemicals to form other chemicals, and that may be the basis for alcohol addiction.

Well, that theory did not hold up. But what struck me was—and it didn't hold up because your liver is making acetaldehyde, and by the time it gets to the brain, it is all chewed up anyways—but here you have a situation where aldehyde is going right into the lung.

And there are only three ways to get things into the brain quickly. One is you put it in the brain, the second fastest way is you put it in the lung, and the third fastest way is you put it in the heart. So it struck us that this compound was getting in the brain, maybe it's doing something that has reinforcing effects.

Mr. WAXMAN. And I want to show you a chart, which I'd like to have entered into the record, without objection, as Exhibit 22. It's made from a slide of your acetaldehyde work.

[Exhibit 22 follows:]


600
520
440
360
280
200
120
40
LEVER PRESSES
NICOTINE (μg/kg) 8.0 8.0 8.0 0 8.0
ACETALDEHYDE (μg/kg) 8.0 0 8.0 8.0 8.0

Mr. WAXMAN. Will you tell us what kind of tests you did on acetaldehyde and what the graph represents?

Mr. DENOBLE. This work was reasonably late in the development of the acetaldehyde self-administration procedures. We demonstrated that acetaldehyde, like nicotine, would maintain behavior and would be reinforcing in rats.

This particular slide looks at the interactions between acetaldehyde and nicotine. If you give a rat—if you would focus on the second bar where it has 8.0 and below it there is a zero, that is 8 micrograms of nicotine. And that will maintain about 100 injections per day.

If you go now to the fourth bar, again, the zero and the 8, that is 8 micrograms of acetaldehyde. That maintains, it looks like, around 230, I guess, injections a day. If you now put them together as in the first, third, and the fifth bar, they interact, and the animal presses a lot more than it would have pressed for either one alone.

This was a demonstration that nicotine and aldehyde combinations are more reinforcing than either of the drugs alone. They interact behaviorally.

Mr. WAXMAN. That is a significant finding, isn't it? It confirmed that if you have cigarettes, not just with the nicotine but the acetaldehyde, that it is even more addictive than nicotine by itself, and there is this reinforcement. Is that a correct statement?

Mr. DENOBLE. It leads to some interesting speculations about the role of nicotine and aldehyde in cigarette smoke. Importantly, very importantly, all the work that we did, most, if not all of it has been replicated by other researchers around the world, even though we had not published it.

This work has never been replicated, so I think we have to look at this as really a scientific inquiry. But it does raise some fascinating possibilities.

Mr. WAXMAN. Well, it means that even for animal tests, we're looking at the addictive nature of nicotine, that nicotine with acetaldehyde is even more of a reinforcer, more of an addicting substance, is that in combination?

Mr. DENOBLE. In this experiment, that is correct.

Mr. WAXMAN. And Philip Morris, rather than encouraging this kind of finding to be made known to the world, what did they do?

Mr. DENOBLE. This was a very high priority project. We were not allowed to even discuss this outside of the research center. We were permitted to give talks on nicotine, but never on acetaldehyde.

Mr. WAXMAN. And this has never been published before?

Mr. DENOBLE. No, sir. Never.

Mr. WAXMAN. I want to leave the area of the work that you did, the two of you, on nicotine and acetaldehyde. I want to ask you about the work of other scientists that you may have observed or known about at Philip Morris. I begin with the dangers of exposure to environmental tobacco smoke.

As you may know, the entire tobacco industry, including Philip Morris, maintains that exposure to environmental tobacco smoke is not a health risk. Dr. DeNoble, while you were at Philip Morris, was anyone conducting research on the effects of exposure to envi-

ronmental tobacco smoke or what is also known as side-stream smoke?

Mr. DENOBLE. Can you give me a moment, please, Sir? Can I take a moment?

Mr. WAXMAN. Yes.

[Mr. DeNoble confers with Mr. Mele.]

Mr. DENOBLE. We are aware of a research project using a plant called Tradesscantia. And the goal of that project was to look at the effects of side-stream smoke on the plant's ability to either reproduce or repair itself.

Mr. WAXMAN. Do you know who was conducting that research project?

Mr. DENOBLE. I don't know the specific name. It was under the control of Dr. Jim Charles in the biochemistry department, but I cannot remember the specific scientist's name.

Mr. WAXMAN. OK. Dr. Mele, do you have any information on that?

Mr. MELE. It was, I believe, Dr. Terry Loo, or Terry Woo, a female researcher.

Mr. WAXMAN. And what do either of you know about this research? What can you tell us about it?

Mr. MELE. I remember one briefing of the biochemical research division where slides were presented of these plants in closed containers. The plants exposed to the side stream smoke were seriously debilitated, wilted, and so forth. Plants exposed to—it was either mainstream smoke or fresh air—I believe there was a comparison between side stream and mainstream—were less debilitated, indicating that side stream smoke was more toxic to these plants.

Mr. WAXMAN. Toxic. Did it create any genetic changes or did it simply kill the plant?

Mr. MELE. Well, just the way they looked, just visually they were wilted and falling over and that sort of thing.

Mr. WAXMAN. And what happened to the work that you are describing? Did Philip Morris allow this important work to be published, or do you know whether it suppressed publication of that?

Mr. MELE. My understanding is that work stopped. If it continued, we didn't know anything about it.

Mr. WAXMAN. Let me ask you about other tests sponsored by Philip Morris on the effects of painting components of tobacco smoke on the skin of mice. Tell us about that, whatever you know about it?

Mr. MELE. I'm just aware that those studies were performed. Dr. Jim Charles worked with another scientist before I was there, I believe. Those studies were more or less commonly discussed in the cafeteria. I never saw any data or evidence of those studies, and I don't know what happened to those studies.

Mr. WAXMAN. Dr. DeNoble, did you ever see a presentation on this research?

Mr. DENOBLE. Yes, I did. The research was conducted at a contract laboratory facility outside of Philip Morris. The purpose of the study was to investigate various components of smoke that had been liquefied on mouse skin. It's a test for carcinogenic activity.

I'm not a teratologist, and I can't interpret that data, but I do remember seeing the slides and hearing the presentation.

Mr. WAXMAN. And what did the mice look like?

Mr. DENOBLE. A lot of the mice had fairly open lesions and wounds from a variety of substances placed on their skin, but I do not know what those substances were, other than they were smoke components.

Mr. WAXMAN. And would nitrosamines have been involved in that?

Mr. DENOBLE. Nitrosamines? No, that was a different research project. That was Dr. Jim Charles' research project. They were looking at the effects of nitrosamines on the lung's ability to repair itself using a chromatid exchange procedure in the lung. Again, that is out of the area of my expertise. I attended some meetings and presentations, but I couldn't give you the——

Mr. WAXMAN. And do you recall what results there were from these nitrosamine studies?

Mr. DENOBLE. In general terms, that the lung's ability to repair itself was impaired after exposure to various nitrosamines.

Mr. WAXMAN. An issue that has received some attention recently is whether the FTC—Federal Trade Commission—test method accurately measures the amount of nicotine consumed by smokers. At our March 25th hearing, Dr. Kessler said that this test method doesn't accurately measure actual consumption because the tobacco companies can manipulate the test.

One example of manipulation he cited was putting ventilation holes in cigarettes which are then covered up by the smoker's lips or fingers. Did either of you observe any research conducted by Philip Morris on this issue?

[Mr. DeNoble and Mr. Mele confer.]

Mr. DENOBLE. There was some research that was done and, again, I'm a little vague on the specific results of the research. At the time there was a cigarette on the market that either had ventilation holes or tubes inserted—not tubes, they were tube-like—what do you call it?

Mr. MELE. Channels.

Mr. DENOBLE. They were channels inserted in the filter, and that would allow a smoking machine to smoke the cigarette without crushing the filter. Research at Philip Morris was done where they actually observed, they filmed people smoking and they noticed that the people would actually crush these channels as they would put the cigarette to their mouth.

Not everybody would do that, but there was evidence of a fair number of smokers delivering a lot more of the smoke phase to the lung than would be delivered in the machine.

Mr. WAXMAN. Do either of you recall the names of any of the researchers?

Mr. DENOBLE. The name was Frank Ryan, Francis Ryan.

Mr. WAXMAN. And what they determined was that some smokers did cover up the ventilation holes with their fingers or their lips, so that the FTC tests which didn't do that might have had a different result than what was the actual consumption of the smoke in the individual involved?

Mr. DENOBLE. That was the general conclusion. That work was also under the control of Dr. Bill Dunn.

Mr. WAXMAN. Thank you. Mr. Bliley?

Mr. BLILEY. Thank you, Mr. Chairman. The only thing I'd like to point out, we had a lot of talk today about contracts. I have an employee agreement here by Abbott Laboratories, and I'd just like your unanimous consent to insert it in the record and to read just a little bit of it?

Mr. WAXMAN. Without objection, it will be received for the record.

Mr. BLILEY. It goes on to say what the employees will do, and the second paragraph, it says, "All memorandum, notes, records, reports, photographs, drawings, plans, papers, or other documents made or compiled by or made available to employee during the course of employment with Abbott, and any copies or abstracts thereof, whether or not they contain confidential information are and shall be the property of Abbott, and shall be delivered to Abbott by employee immediately upon termination of employment with Abbott." So I just mention that to say that it's not uncommon to have contracts of confidentiality with employees. Thank you, Mr. Chairman.

Mr. WAXMAN. Thank you, Mr. Bliley. Mr. Wyden?

[Testimony resumes on p. 147.]

[The employee agreement referred to follows:]

EMPLOYEE AGREEMENT

AGREEMENT made between ABBOTT LABORATORIES ("ABBOTT"), and the undersigned employee ("EMPLOYEE"), WITNESS the following:

EMPLOYEE is engaged by ABBOTT in a position of trust and confidence in which EMPLOYEE may use, observe, or obtain Confidential Information.

EMPLOYEE, by reason of the nature of EMPLOYEE's duties, will be provided with information and/or facilities and equipment which may enable EMPLOYEE to make discoveries, inventions, improvements, or innovations useful to ABBOTT or its subsidiaries or affiliated companies.

It is to the mutual benefit of ABBOTT and EMPLOYEE that ABBOTT protect its rights in Confidential Information and obtain the benefit of discoveries, inventions, improvements, and innovations developed by its employees.

In consideration of the execution of this Agreement by other key employees of ABBOTT, the mutual agreements contained herein and in consideration of the present and future employment of the EMPLOYEE by ABBOTT, it is agreed:

1. "Confidential Information" shall mean methods, processes, techniques, shop practices, formulae, compounds, compositions, organisms, equipment, research data, clinical and pharmacological data, marketing and sales information, personnel data, customer lists, financial data, plans and all other know-how and trade secrets which are in the possession of ABBOTT, or any of its subsidiaries or affiliated companies, and which have not been published or disclosed to the general public.

2. All memoranda, notes, records, reports, drawings, [redacted] compiled by or made available to EMPLOYEE during the term of employment with ABBOTT [redacted] or abstracts thereof, whether or not they contain Confidential Information, are and will be the property of ABBOTT and shall be delivered to ABBOTT by EMPLOYEE immediately upon termination of employment with ABBOTT.

3. All discoveries, inventions, improvements, and innovations, whether patentable or not (including all data and records pertaining thereto), which EMPLOYEE may invent, discover, originate, or conceive during the term of employment with ABBOTT, and which in any way relate to or are or may be useful in connection with the business of ABBOTT or any of its subsidiaries or affiliated companies, shall be the sole and exclusive property of ABBOTT. EMPLOYEE shall promptly and fully disclose each and all such discoveries, inventions, improvements, or innovations to ABBOTT.

4. EMPLOYEE shall assign to ABBOTT EMPLOYEE's entire right, title, and interest to any of the discoveries, inventions, improvements, and innovations described in Paragraph 3 of this Agreement and any related U.S. or foreign patents and patent applications; shall execute any instruments considered necessary by ABBOTT to convey or perfect ABBOTT's ownership thereof; and shall assist ABBOTT in obtaining, defending and enforcing its rights therein. ABBOTT shall bear all expenses it authorizes be incurred in connection with such activity and shall pay to EMPLOYEE reasonable compensation for any time spent by EMPLOYEE performing such duties at the request of ABBOTT after termination of employment.

5. EMPLOYEE shall not, without the written consent of ABBOTT, during the term of employment with ABBOTT or thereafter, use for the benefit of EMPLOYEE or others, or disclose to others, any Confidential Information obtained during the course of employment with ABBOTT.

ABBOTT, for a period of one year after the termination of employment with ABBOTT, engage directly or indirectly, for the benefit of EMPLOYEE or others, in any activity or employment in the faithful performance of which it could be reasonably anticipated that EMPLOYEE would be required or expected to use or disclose any Confidential Information obtained during the course of employment with ABBOTT. This covenant shall not be construed to limit in any way EMPLOYEE's obligation not to use or disclose Confidential Information as set forth in Paragraph 5 above.

7. This Agreement shall not be construed to limit in any way any "shop rights" or other common law or contractual rights of ABBOTT, in or to any discoveries, inventions, improvements, and innovations, and in or to any Confidential Information which ABBOTT has or may have by virtue of EMPLOYEE's employment.

8. It is understood that either ABBOTT or EMPLOYEE may terminate the employment relationship at any time. Upon such termination EMPLOYEE shall advise ABBOTT of the name and address of EMPLOYEE'S intended future employer. The parties' obligations under this Agreement shall survive such termination of employment.

9. If any provision or provisions of this Agreement shall be held to be unenforceable by any court, the remaining provisions shall be unaffected and shall continue in full force and effect. This Agreement shall inure to the benefit of and be binding upon ABBOTT, its successors and assigns and EMPLOYEE, EMPLOYEE's heirs, executors, and administrators.

.....
Witness

.....
Employee

.....
Address

ABBOTT LABORATORIES

Dated, ... 19 .....
at North Chicago, Illinois

By.....

I acknowledge receipt of and agree to comply with the following:

1. A Guide to the Corporate Antitrust and Conflict of Interest Policies;
2. Corporate Policy No. 34-7, Illegal Political and Governmental Payments;
3. Corporate Policy No. 34-8, Entertainment, Gifts and Facilitating Payments;
4. Corporate Policy No. 30-1, Requirements for Release of Confidential Information; and
5. Corporate Policy No. 34-9, United States Political Contributions.

Employee

Employee Number

3813-R4

CELANESE

CELANESE CORPORATION

CONFIDENTIAL INFORMATION AND INVENTIONS AGREEMENT

The undersigned (herein called "the Employee"), as a condition of his employment or continued employment by Celanese Corporation (herein called "the Company") agrees as follows:

1. The Employee shall not for any reason nor at any time disclose to any person (except to the extent that the proper performance of his duties may require such disclosure to other employees of the Company) any secret or confidential information relating to the processes, products, machinery, apparatus or trade secrets of the Company or of any affiliated corporation, or any other confidential information given him by any officer, employee or representative of the Company or obtained in the course, or as a result, of said employment, unless so authorized in writing by an officer of the Company. Any information not generally available to the public shall be considered secret or confidential for the purposes of this Agreement.

2. The Employee shall communicate at once to the Company, all inventions and improvements which, while this employment continues, he may conceive, make or discover that relate in any way to the processes, products, machinery or plants of the Company or to any of the operations in which the Company or any subsidiary or affiliated corporation has been or is engaged at the time, and such inventions and improvements shall become the exclusive property of the Company without any obligation on the part of the Company to make any payment therefor in addition to the salary of the Employee. The Employee shall, at the request of the Company either during or after termination of this employment, execute patent applications and assignments thereof relating to such inventions and improvements and powers of attorney relating thereto for any Country and shall take all such other actions as the Company may require to maintain and protect them. The Company shall pay all costs and charges incurred in protecting such inventions and improvements if it desires to protect them.

3. The Company may assign this Agreement to any subsidiary or affiliated corporation or to the transferee of the whole or any part of its business and nothing contained herein shall affect the Company's right to terminate the employment of the Employee. Termination of such employment shall not relieve the Employee from any of his obligations, under Paragraph (1) hereof, not to disclose information or, under Paragraph (2) hereof, to communicate and protect inventions and improvements conceived or made during his employment.

4. On the termination of his employment for any reason, the Employee shall forthwith quit the Company's premises and shall deliver up to the Company all documents, plans, drawings or papers in any way relating to the affairs of the Company, or any subsidiary or affiliated corporation, which may be in his possession or under his control.

Date

Employee Signature

FORM CEC-1577 REV. 6-66

THE DOW CHEMICAL COMPANY

The basis of Dow's success resides in its employees and the technology and related information which they generate. The continued growth of Dow depends on its ability to maintain its competitive edge which not only requires the generation of new technology but equally the protection of its existing technology. In addition to technology, Dow has developed expertise and generated confidential information in the manner in which it conducts its business. This, too, is know-how and information which is treated by Dow as confidential.

As an employee of Dow you will or have become familiar with trade secrets, Dow know-how and other confidential information relating to Dow's business, products, processes and developments. You may generate or have generated such confidential information yourself. In order that you fully understand and accept your responsibilities as a Dow employee, you are asked to review and agree to the terms printed below by signing this agreement.

EMPLOYEE AGREEMENT

I, _____, in consideration of my employment or continued employment by The Dow Chemical Company or any of its wholly owned subsidiaries*, collectively called "Dow" hereafter, the salary or wages, salary raises and promotions and other benefits received by me during such employment and in consideration of being given access to confidential information when required, hereby agree as follows:

Article 1 — Confidential Information

Other than as required in my duties as an employee of Dow, I shall not disclose to anyone or use either during or after my employment, except with the written consent of Dow, any trade secret, know-how or confidential technical or business information of Dow.

The same obligation shall apply to any trade secrets or other confidential information of any third party learned by me as a Dow employee and with respect to which Dow has an obligation to maintain such in secrecy.

As a Dow employee, I shall not use or disclose to Dow any trade secret or other confidential technical and business information of any previous employer or other third party to whom I have an obligation of secrecy.

Article 2 — Inventions and Discoveries

All inventions and discoveries including those in formative stages, made by me, solely or jointly with others, and pertaining to Dow's business, processes, products, developments and research activities shall be the property of Dow.

I will maintain accurate and complete written records and promptly, without request, disclose to Dow all such inventions and discoveries made by me alone or jointly with others.

Article 3 — Patents

Upon request of Dow and at Dow's expense, I or my legal representative will assign and convey to Dow my entire right in and to any

* Subsidiaries which have their own employee agreements are not included hereunder.

... and ... Article 2; assist Dow and its agents in preparing patent applications in all countries of the world relating to the same; sign and deliver to Dow all papers necessary thereto including assignments of patent applications and patents; and will give all information and testimony, sign all papers and do all things which may be needed or requested by Dow to obtain, extend, reissue, maintain or enforce such patents. When any assistance relating to such patents or patent applications is rendered after my employment, Dow will pay me a reasonable sum, as determined by Dow, for my time and expenses.

Article 4 — Documents

I acknowledge that all originals and copies of drawings, blueprints, manuals, reports, notebooks, notes, photographs and any other recorded, written or printed matter relating to research, manufacturing operations or business of Dow made or received by me during my employment are the property of Dow and I will destroy or surrender such at the request of Dow, but in any event no later than the termination of my employment. I will similarly return all other property of Dow such as equipment, samples, models and biological cultures.

Article 5 — Notification

For a period of five years after termination of my employment with Dow, I agree to inform Dow of any employment, including any consultantship, I accept which involves an area of technology or business in which I worked for Dow in the last five years of my employment at Dow, before entering into such employment.

Article 6 — Acceptance

I have read this Agreement carefully and I understand and accept it. It is to be retroactive to the date of my first employment by Dow and is in addition to any rights and obligations of myself and Dow under any previous employee agreement signed by me.

I understand that in the event that Dow should waive any part of this Agreement or that any part should be determined to be unenforceable, I am not thereby relieved from the remaining provisions of the Agreement.

My obligations hereunder will continue in the event I am transferred to a different location or assignment by Dow and after termination of my employment with Dow.

Dated ______________ Signed ______________________

Master No. ______________________

Division, Department or Subsidiary ______________________

Location ______________________

Witness ______________

FORM C-4846 ... STOCKED UNDER FORM NO. ...

KOPPERS

EMPLOYMENT AGREEMENT

(IMPORTANT – READ CAREFULLY)

WHEREAS the undersigned is employed or is about to be employed by KOPPERS COMPANY, INC. or a subsidiary of KOPPERS COMPANY, INC. (said subsidiary is hereby defined as a company of which KOPPERS COMPANY, INC. owns, directly or indirectly, at least fifty per cent (50%) of the voting stock, both KOPPERS COMPANY, INC. and subsidiary being hereinafter collectively and/or separately referred to as "KOPPERS" whichever reference is or becomes appropriate to the employment of the undersigned) and is desirous of obtaining or continuing said employment, and is affected, in the course of his employment, opportunities to become familiar with the technical and industrial practices and, to various extents, with confidential information of KOPPERS, and has or will have the opportunity of using KOPPERS' tools, appliances, facilities and technical information.

NOW, THEREFORE, in consideration of the premises and of said employment and the salary paid therefor, the undersigned does hereby agree with KOPPERS that:

He shall, while in the employ of KOPPERS, use his best efforts and skill in perfecting and devising processes, apparatus and products pertaining, relating or applicable in any way to any business or investigation in which KOPPERS is or hereafter may be engaged or interested, and shall, as one of his duties, where possible, make suggestions for improvements, patentable and otherwise, in KOPPERS' operations;

He shall not use or disclose to others outside KOPPERS without specific authorization by KOPPERS, confidential information received by him from or for KOPPERS;

All inventions conceived or made by him during the term of his employment with KOPPERS relating to the fields of the industrial and research activities of KOPPERS during that time, and all patents, domestic and foreign, upon said inventions shall be the sole property of KOPPERS;

Accordingly, he shall promptly and fully disclose to KOPPERS all such inventions conceived or made by him during his term of employment with KOPPERS and shall, upon request made at any time hereafter, assign such inventions to KOPPERS, aid in the prosecution of patent applications and promptly execute all papers necessary to the filing and prosecution of patent applications, involving patent interferences, and to the enforcement of patents on such inventions, without any further compensation than payment for employment;

In the event that KOPPERS has not indicated a desire to use or to retain its rights to an invention conceived or made by the undersigned during said employment, he may at any time after making a full written disclosure of said invention to KOPPERS, direct a written request to the KOPPERS Patent Section for the release of said invention; but in the event such a release is granted, KOPPERS and its successors and customers shall not be liable at any time for any practice of said invention;

He shall, at KOPPERS' request, testify in any proceeding or suit which may arise in connection with any of his sole or joint inventions; provided that for any such testifying, after termination of his employment with KOPPERS, he shall be paid at the rate of at least fifty dollars ($50.00) per day for time he actually spends in testifying, and provided that all of his expenses, attendant upon such proceedings or suit, are borne by KOPPERS;

He shall, upon termination of employment with KOPPERS, turn over to KOPPERS all notes, memoranda, notebooks, drawings and other records in connection with his employment specifically covered by the third paragraph, hereto; it being understood that these records and the information contained thereon are at all times the sole property of KOPPERS;

He represents that he has no agreement with others which will interfere with the operation of this agreement;

This agreement shall inure to the benefit of and shall be binding upon KOPPERS, its successors and assigns and upon the undersigned, his heirs, representatives, administrators, executors, and assigns.

IN TESTIMONY WHEREOF, the undersigned, intending to be legally bound hereby, has affixed his signature and seal this _____ day of _____, 19__

_____ (SEAL)

PETROLITE CORPORATION

EMPLOYEE PATENT AND CONFIDENTIAL INFORMATION AGREEMENT

TO PETROLITE CORPORATION, its subsidiaries:
International Pollution Control, Inc.
Petrolite Anlagenbau-und Vertriebsgesellschaft m.b.H.,
Petrolite Corporation of Canada, Ltd., Petrolite France S.A.,
Petrolite International Corporation, Petrolite Limited,
South American Petrolite Corporation, and any other subsidiary
of said Petrolite Corporation.

In consideration of my employment or continued employment in any capacity by the company (which term includes Petrolite Corporation, its subsidiary corporations or divisions and its successors) and in consideration of the salary, wages or other compensation paid for my services in the course of such employment, I agree:

(A) To communicate promptly to the company all inventions, discoveries and improvements (whether or not they are patentable) conceived or reduced to practice by me, solely or in collaboration with others, from the time of entering the company's employ until I leave (1) which are useful in the business, work or investigations of the company, or (2) which result from or are suggested by any work which I may do for or on behalf of the company (if an application for patent for any such invention, discovery or improvement be made by me within six (6) months after I leave the company's employ, such invention, discovery or improvement shall be presumed to have been conceived during the period of my employment).

(B) To assist the company during and subsequent to such employment in every proper way (without charge to the company but at its expense) to obtain patents or otherwise protect such inventions, discoveries and improvements in any and all countries against appropriation by others; all such inventions, discoveries and improvements (whether patented or not) and any patents that may issue thereon to be the sole and exclusive property of the company and being hereby assigned thereto; and for the purpose of this clause to execute and do all such documents, acts and things as the company may deem necessary or desirable.

(C) To make and maintain adequate and current written records of all such inventions, discoveries and improvements, in the form of notes, sketches, drawings, or reports relating thereto, which records shall be and remain the property of and available to the company at all times.

(D) Except as the company may otherwise consent in writing, not to disclose or to discuss with others outside the company at any time (except as my company duties may require) either during or subsequent to my employment, any information, knowledge or data of a confidential nature I may receive during the course of my employment relating to the company's business procedures, formulae, methods, machines, manufactures, compositions, inventions, discoveries, improvements or other matters of a confidential nature. (The aforesaid term "confidential" is used in its ordinary sense and does not refer to any Governmental security classification).

. . notify . . writing before I make any disclosure or perform or cause to be performed any work for or on behalf of the company which appears to threaten conflict with:

(1) rights I claim in any invention, discovery, or improvement -

(a) made by me or others prior to my employment, or

(b) otherwise outside the scope of this agreement, or

(2) rights of others arising out of obligations incurred by me -

(a) prior to this agreement, or

(b) otherwise outside the scope of this agreement.

In the event of my failure to give notice under the circumstances specified in (1) of the foregoing, the company may assume that no such conflicting invention, discovery or improvement exists, and I agree that I will make no claim with respect thereto.

This agreement may not, on behalf of or in respect to the company, be changed or modified or released, discharged, abandoned or otherwise terminated, in whole or in part, except by an instrument in writing signed by the President or other authorized executive of the company.

This agreement shall be binding upon my heirs, executors, administrators or other legal representatives or assigns.

I represent that except as stated on the reverse of this agreement I have no agreements with or obligations to others in conflict with the foregoing.

_____
Witness (The employee's immediate superior or other appropriate representative of the company)

_____
Witness' Position

Attest:

_____
Secretary

Attest:

_____
Secretary

_____
(Employee sign first and last names in full)

Date:
(To be written in by Employee)

Accepted: PETROLITE CORPORATION

_____
Vice President

Date: _____

Accepted: _____
(Subsidiary, if any)

By _____

_____
(Position)

Date: _____

Employment Agreement

In consideration of my employment by Rohm and Haas Company and the compensation and benefits attendant thereto, I agree as follows:

I. I recognize that any business or trade secrets, including secret processes of manufacture of Rohm and Haas Company, are the property of Rohm and Haas Company, as well as any information contained in research records, financial records, payroll records, personnel records, and all other confidential information to which I have access. I agree to keep such information secret and confidential and not to use such information other than in an authorized manner in the course of Rohm and Haas Company's business. I further agree not to divulge such information to outsiders or other unauthorized persons either while employed by Rohm and Haas Company or afterwards.

II. I will not engage in any business interests or business activities which, in the opinion of Rohm and Haas Company, conflict with the interests of Rohm and Haas Company.

III. I will disclose promptly to Rohm and Haas Company any and all inventions, discoveries, and improvements (patentable or not) conceived or made by me during the period of my employment and relating to the business or activities of Rohm and Haas Company. I hereby assign and agree to assign all of my interest therein to Rohm and Haas Company or its nominee, and agree to execute any and all documents necessary to enable Rohm and Haas Company to secure Letters Patent of the United States or any foreign country or to otherwise protect Rohm and Haas Company's interest therein. These obligations shall continue beyond the termination of my employment with respect to inventions, discoveries, and improvements conceived or made by me during the period of employment.

IV. I agree, on termination of my employment, to return to Rohm and Haas Company all papers, notes, books, or other documents or property belonging to Rohm and Haas Company or relating to its business.

Executed in _____, this _____ day of _____

_____ (SEAL)
SIGNATURE

ROHM AND HAAS COMPANY

_____
WITNESS

_____

Form 668 REV. 8/67

EMPLOYEE
PROPRIETARY INFORMATION AND CONFLICT
OF INTEREST AGREEMENT

In consideration of my employment by Spencer Kellogg Division of Textron Inc., a Delaware Corporation (the "Company"), and of the compensation received therefor, I agree:

1.(a) During and subsequent to the period of my employment, I will communicate promptly and fully to the Company all inventions, discoveries, improvements or designs conceived or reduced to practice by me during the period of my employment (alone or jointly with others), and, except as provided in paragraph 1.(b) below, I will and hereby do assign to the Company and/or its nominees all my right, title and interest in such inventions, discoveries, improvements or designs and all my right, title and interest in any patents, patent applications or copyrights based thereon without obligation on the part of Company to make any further compensation, royalty or payment to me. I will assist the Company and/or its nominees (without charge but at no expense to me) at any time and in every proper way to obtain and maintain for its and/or their own benefit patents for all such inventions, discoveries or improvements and copyrights for all such designs.

1.(b) This agreement, however, does not obligate me to assign to the Company any invention, discovery, improvement or design which, in the judgment of the Company, does not relate to the business efforts or research and development efforts in which, during the period of my employment, the Company is actually engaged or reasonably would be expected to become engaged.

2. Except as my duties during my employment with the Company may require or as the Company may otherwise consent in writing, I will not at any time disclose or use, either during or subsequent to my employment, any information, knowledge or data I receive or develop during my employment which is considered proprietary by the Company or which relates to the trade secrets of the Company as contained in formulas, business processes, methods, machines, manufacturing processes, compositions, inventions, discoveries or otherwise or which the Company has received in confidence from others. Neither will I disclose to the Company or induce the Company to use any proprietary information or trade secrets of others except as may be properly received by me in connection with my employment for disclosure to or use by the Company.

3. During the period of employment, I will not independently engage in the same or similar lines of business or research as that carried on by the Company, or directly or indirectly, serve, advise or be employed by any individual, firm or corporation engaged in the same or a similar line of business or research as that carried on by the Company.

4. As used herein, Company shall mean the Division or subsidiary of Textron Inc. identified above and any subsidiary corporation, Division or unit administratively affiliated with the Company.

5. My obligations hereunder may not be changed or modified, released, discharged, abandoned or terminated, in whole or in part except by an instrument in writing signed by an officer of the Company.

6. This agreement shall be binding upon my heirs, personal representative, successors and assigns.

7. Except as set forth below, I have no agreements with, or obligations to others, in conflict with the foregoing and I do not own or have an interest in any patent, patent application, copyright or unpatented inventions.

8. Upon any termination of my employment, I shall return all proprietary or nonpublic records and documents of or pertaining to the Company then in my possession, and shall not make or retain any copy or extract thereof.

9. Any prior agreements between us relating to patents, copyrights, trade secrets, proprietary information or conflict of interest with the Company are hereby superseded.

_____ (Date)

_____ (Employee signature)

_____ (Signature of witness)

_____ (Employee name - please print)

INFORMATION REQUIRED BY PARAGRAPH 7 OF THE FOREGOING PROPRIETARY INFORMATION AND CONFLICT OF INTEREST AGREEMENT.

List here any items which are exceptions under paragraph 7 (agreements with or obligations to others and patents):

Mr. WYDEN. One last point, Mr. Chairman.

First, let me thank both of you because I think this has been very helpful. I want to ask you one last question. As I have worked on Chairman Waxman's subcommittee over the years on this issue, we have continually heard that the tobacco industry's position is that smoking is essentially a matter of free choice.

I think, you know, that we had some science that has raised questions about that, but certainly at a minimum if it is a matter of free choice, people ought to be in a position to make an informed choice.

One of the things that has troubled me is it seems to me that if your studies had gotten out at the time that they were written, at a minimum, at a bare minimum, other scientists would have followed up on the research that you had done. And then, clearly, the American people could have made a more informed choice about smoking. Would you agree with that, Dr. DeNoble?

Mr. DENOBLE. Yes, I do agree with that. It was the reason that Paul and I took the risk in 1986 to try to publish this material and present it. The scientific community had the right to look at this research and to confirm or disconfirm it. And they confirmed it, much of it, but years after it should have been confirmed.

Mr. WYDEN. Thank you, Mr. Chairman.

Mr. WAXMAN. Thank you, Mr. Wyden.

We've referred to a number of exhibits during this hearing. Let me indicate that all of the exhibits were shared with them I know, in advance of this hearing.

And let me ask unanimous consent, so that we have it on the record, that all those exhibits be made part of the record in the sequential numbering order that they have been referred to. And without objection, that will be the order.

And let me indicate that Dr. DeNoble and Dr. Mele, you not only met with our staff, but you had a meeting with the minority staff, as well, prior to this hearing, is that correct?

Mr. DENOBLE. Yes, that's correct.

Mr. WAXMAN. And that was a private meeting?

Mr. DENOBLE. Yes, it was.

Mr. WAXMAN. OK. I want to make an observation then. I thank you both for being here.

I was taken aback 2 weeks ago when we had at this very table the 7 chief executive officers of the major tobacco companies in this Nation and they gave us blanket denials, absolute blanket denials about a number of important issues.

We asked them if they knew whether cigarette smoking caused people harm, and they said they didn't know. But one thing they did know about and could tell us was that cigarette smoking was not addictive. And we went down the line and each chief executive officer indicated that cigarette smoking was not addictive.

They also told us at this hearing that environmental tobacco smoke is not dangerous, that advertising was not intended to influence kids. One of the witnesses even told us that he thought cigarette smoking was not addictive and, if it was, it was no more of an addiction than eating Twinkies.

Well, I want to just indicate that hearing, as compared to this hearing, is the reason why Congress has got to be involved in the

oversight of what is happening with tobacco in this country. We have heard from tobacco executives who, I believe, are more focused on corporate survival than on corporate responsibility.

Two of the three criteria for drug addiction were known to be present in cigarettes in animal tests as early as 1983, according to the two of you in your testimony today, which is under oath. And not only that, the president of Philip Morris was told this information.

I think there is a code of corporate conduct which we expect every corporation in this country to follow, and that is not to come before the Congress and deny everything and accept no responsibility. I expect this is not our last hearing on this subject

I think we need to get, for the record, a lot of responses to what you had to say. That's only the fair thing to do, but I think we've uncovered enough information for which I think we ought to get a response from these companies, particularly Philip Morris because that is the one that you talked about, but others as well, as to how much they've known, what they knew, and when they knew it, to quote a phrase that's recently been in the news again.

I thank you both for being here. And I want to recognize any other members who want to make any other comments. Mr. Bliley?

Mr. BLILEY. Just clear something up for me, Dr. DeNoble, if you would? In your testimony in response to my questions today, you did say that nicotine as well as acetaldehyde are reinforcing agents, but you also testified that nicotine is not addictive, I believe, is that right?

Mr. DENOBLE. No, sir, that is not correct. What I said was that from an animal study you can't infer addiction. I do think that here is a preponderance of evidence that has come about in the last 14 years to show that nicotine is an addictive substance in humans.

Our data, back in 1982, 1983, and 1984, suggested that from rat studies, but you cannot prove addiction in a rat, but you can say you need to look further.

Mr. BLILEY. And that was the same thing for acetaldehyde?

Mr. DENOBLE. That is correct.

Mr. BLILEY. I see. Thank you very much.

Mr. DENOBLE. You're welcome, sir.

Mr. WAXMAN. Thank you, Mr. Bliley.

Mr. Wyden, anything further?

Mr. WYDEN. On that last point, you are saying you can't prove addiction in people by tests on animals, but you certainly can surmise that there is information there that ought to be pursued to determine whether, in fact, addiction is a reality?

Mr. DENOBLE. Yes. That's a real strong indicator.

Mr. WAXMAN. Let me indicate again the quote from Dr. Ellis, who testified before us. And she said that to her knowledge there is no evidence that nicotine or cigarette smoking plays in any of these definitions, and she was referring—let me read the whole quote:

"The strict pharmacological definition of addiction involves three different criteria. They are intoxication, physical dependence, and tolerance. And to my knowledge there is no evidence that nicotine or cigarette smoking plays in any of these definitions."

I think that goes beyond that very thin cutting of those words that are so carefully crafted, to say something that I believe to be misleading. This is an absolutely untrue statement under anybody's interpretation of the words before us.

Thank you both very much for being here. I want to commend you and thank you for your courage and willingness to come before us. That completes this hearing, and we stand adjourned.

[Whereupon, at 12:35 p.m, the subcommittee was adjourned, to reconvene at the call of the Chair.]

[The following information was submitted for the record:]

ADDITIONAL QUESTIONS FOR DR. VICTOR J. DENOBLE

(1) Please state the name of each employment you have held since 1973, excluding Philip Morris. For each employment, please state the correct company name, address, telephone number, name of supervisor(s), all positions you held, and your reason for leaving.

(2) Please state with respect to all employment you have held since 1973 (excluding Philip Morris) whether you were ever discharged, asked to resign, or otherwise left the employment involuntarily. If so, please describe the circumstances in detail and name your supervisor(s) at the time.

(3) Please state with respect to all employment you have held since 1973 (excluding Philip Morris) whether you were ever counseled or disciplined in any manner for poor performance of any kind, including but not limited to charges of improper research procedure or manipulation of test data or research conclusions. If so, please describe the circumstances in detail and name your supervisor(s) at the time.

(4) Please state with respect to all employment held since 1973 (excluding Philip Morris) whether you ever filed or threatened to file a lawsuit, charge, or other challenge of any kind to any employment action, including but not limited to discharge, demotion, lack of promotion, or performance review. If so, please describe the circumstances in detail, including but not limited to the court or agency where such lawsuits, charges, or challenges were filed.

Victor J. DeNoble, Ph.D.
1200 Camp Woods Court
Newark, Delaware 19711
June 30, 1994

Mr. Thomas J. Bliley, Jr.
U.S. House of Representatives
2241 Rayburn Office Building
Washington, DC 20515-4607

Dear Congressman Bliley:

Thank you for your letter dated June 13, 1994 asking me to respond to additional questions concerning the issue of tobacco and health. In answering your questions, I am compelled to tell you that I am somewhat confused as to the nature and intent of the questions you have forwarded. The questions have no relevance to tobacco and health and represent an inquiry into my employment history before and after Philip Morris. When I was requested to appear before the congressional subcommittee on April 28, 1994, I did so voluntarily and discussed research projects that were performed by me and my colleagues for Philip Morris, Inc. between April 1, 1980 and April 5, 1984. Since the nicotine research has been replicated in laboratories all over the world over the last ten years, there can be no question regarding the validity of the research. With regard to the acetaldehyde data, I understand that Philip Morris has graciously submitted the raw data, as well as, reports to the subcommittee and I encourage the subcommittee to conduct an independent scientific review of my conclusion that acetaldehyde is a reinforcing agent. I am disappointed that the questions provided to me deal exclusively with my work history and do not relate in any way to the information provided to the subcommittee. I question whether other individuals who voluntarily give testimony to the subcommittee are subject to a personal review because their testimony may not suit selected members of that subcommittee. As you will see, my responses to your questions have no bearing on either my testimony given to the subcommittee, on the research performed at Philip Morris

laboratories, or on the validity and reliability of the data collected over a decade ago.

I cannot help but think that the intent of these questions are to seek information to impugn my character, and are a form of punishment for coming forward and telling the truth. When I met with your staff on April 27th, I, in the presence of my wife was told that I had no rights once I appeared before Congress. I am now beginning to understand what they meant.

Respectfully sir, I challenge the intent and motive of your inquiry and further, I question, why you are conducting an investigation of Victor DeNoble instead of an investigation of the issue at hand - tobacco and health.

With all due respect, I feel the American public has a right to know what the consequences may be for coming forward openly and honestly to give testimony before our elected officials.

Mr. Bliley, in my testimony to Congress concerning my research activities at Philip Morris, I gave testimony that was factual, objective, and, with conscious intent, non-judgmental. My testimony reflected what I believe was a positively motivated research program by the Philip Morris organization and I find your questions disappointing. I sincerely hope that other individuals are not treated in the same manner.

Question Number 1:

1973 - 1974: Graduate student, Aldelphi University, South Avenue Garden City, New York. 11530
(516) 877-3000
Research Advisor: Marjorie Kaplan, Ph.D.
Graduated.

1974 - 1977: Senior Research Scientist, Downstate Medical Center, 450 Clarkson Avenue, Brooklyn, New York.
(718) 270-1000
Post-Doctoral Research sponsored by NIAA.
Advisor: Henri Begleiter, Ph.D.
Completed post doctoral research.

1978 - 1980: Research Associate, Psychiatry Research Unit, Mayo Research Building, University of Minnesota, Minneapolis,420 Delaware Avenue SE Minnesota, 55455
(612) 625-5000
Post-Doctoral Research Fellow for the NIDA.
Advisor: Richard Meisch, M.D., Ph.D.
Recruited by Philip Morris Research.

1980 - 1984: Associate Senior Scientist, Behavioral Pharmacology Laboratory, Philip Morris Research Center, Richmond, Virginia.
Supervisors: William Dunn, Ph.D., Jim Charles, Ph.D.
Laboratory closed.

1984 - 1987: Research Associate, Ayerst Laboratories Research, Inc., Princeton, CN 8000 New Jersey.08543
(908) 329-2300
Supervisor: Kevin Keim, Ph.D.
Recruited by DuPont Pharmaceuticals.

1987 - 1992: Manager, Development and Training, R&D Operations The DuPont Merck Pharmaceutical Company, Experimental Station, Wilmington, Delaware.
(302) 892-0805
Supervisors: Thomas Bernadzikowski, MA., George Steinfels, Ph.D., Len Cook, Ph.D
Wrongfully terminated

1992 - Present: Senior Behavior Analyst, Department of Mental Retardation, 1901 DuPont Highway, Wilmington, Delaware.19720
(302) 577-4928
Supervisor: Scott Daner, MA.
Still there.

Question Number 2:

I have not been discharged, asked to resign or left employment involuntarily with the exception DuPont Merck who I have filed a lawsuit against. See answer to Question Number 4.

Question Number 3:

I have not been counseled for poor performance of any kind, including, but not limited to, charges of improper research procedure or manipulation of test data or research conclusions at any of the positions that I have held. In fact, I have been given outstanding reports of my research and management skills, as well as, accomplishment awards for outstanding scientific contributions.

Question Number 4:

I have filed a lawsuit against DuPont Merck for wrongful termination in the Superior Court of Delaware. I expect that this lawsuit will come to conclusion within a year. As I do not wish to jeopardize any legal position that I may have, I suggest you address further questions directly to my counsel, Mr. Bayard Snyder, Esq., Suite 830, PNC Bank Building, 300 Delaware Avenue, Wilmington, Delaware, 19899. Telephone Number: (302) 657-8300.

In addition to the above positions, I have also held adjunct teaching positions at the following universities or colleges: University of Delaware, 1989-1990, Trenton State College, 1986-1987, Virginia Commonwealth University, 1983-1986, State University of New York, 1976-1978, City University of New York,1976-1978. The answer to questions two and three apply to these positions as well.

I have addressed your questions to the best of my knowledge and I would welcome any further questions related to issues before the subcommittee.

Respectively,

Victor J. DeNoble, Ph.D

LIST OF DOCUMENTS WHICH HAVE BEEN RETAINED IN COMMITTEE FILES

On May 9, 1994, Philip Morris submitted additional documents to the Subcommittee that pertain to the work of Dr. DeNoble. The following documents from Philip Morris have been made part of the record for this hearing and are available for review by the public at the office of the Committee on Energy and Commerce and the office of Representative Henry A. Waxman:

Philip Morris Interoffice Correspondence, Discrimination Studies, May 7, 1980.

Philip Morris Interoffice Correspondence, Possible Restructuring of the Behavioral Research Lab, June 18, 1980.

Philip Morris Interoffice Correspondence, Research Progress Concerning Discrimination and Prostration Studies, August 18, 1980.

Philip Morris Interoffice Correspondence, The Behavioral Pharmacology Program, October 14, 1980.

Philip Morris Interoffice Correspondence, Progress in Behavior Pharmacology Laboratory, March 27, 1981.

Philip Morris Research Center Manuscript Review Board Information Sheet, Studies on the Effects of Intraventricular Infusions of (-)-Nicotine on Behavior Maintained under Fixed Ratio Schedules, January 20, 1981.

Philip Morris Interoffice Correspondence, Progress Report, August 24, 1981.

Philip Morris Research Center Manuscript Review Board Information Sheet, Brain Sites Involved in the Mediation of the Behavioral Effects of Intraventricularly Administered (-)-Nicotine, March 1982.

Article published in Psychopharmacology, Behavioral Effects of Intraventricularly Administered (-)-Nicotine on Fixed Ratio Schedules of Food Presentation in Rats, by Victor J. DeNoble, Yvonne Dragan, and Lisa Carron, Spring 1982.Philip Morris Interoffice Correspondence, Progress Report, April 21, 1982.

Philip Morris Interoffice Correspondence, Project Number 1610 (Behavioral Pharmacology) Objectives and Plans--1982-1983, July 20, 1982.

Philip Morris Interoffice Correspondence, Promotion of Dr. Victor J. DeNoble to Associate Senior Scientist, March 1, 1983.

Philip Morris Interoffice Correspondence, Behavioral Pharmacology Annual Report--1983, June 1, 1983.

Philip Morris Interoffice Correspondence, Prostration and Discrimination Tests, June 14, 1993.

Philip Morris Interoffice Correspondence, Project 1610 (Behavioral Pharmacology) Objectives and Plans, 1984, September 6, 1983.

Termination of Chronic Acetaldehyde Administration Does Not Result in a Physical Dependence Syndrome, Philip Morris Research Center, (not dated).

Philip Morris Research Center Manuscript Review Board Information Sheet, Effects of Chronic Nicotine Administration and Its Termination on Schedule-Controlled Behavior in Rats, (not dated).

Nicotine as Positive Reinforcer for Rats: Effects of Infusion Dose and Fixed Ratio Size, Victor J. DeNoble, Paul C. Mele, and Francis J. Ryan, Philip Morris Research Center, (not dated).

Development of Behavioral Tolerance Following Chronic Nicotine Administration, Paul C. Mele and Victor J. DeNoble, Biochemical Research Division, Philip Morris Research Center, (not dated).

Federation of American Societies for Experimental Biology, Federal Proceedings, Abstracts, 70th Annual Meeting, St. Louis Missouri, April 13-18, 1986, Volume 45, Number 3, March 1, 1986.

REGULATION OF TOBACCO PRODUCTS

TUESDAY, MAY 17, 1994

HOUSE OF REPRESENTATIVES,
COMMITTEE ON ENERGY AND COMMERCE,
SUBCOMMITTEE ON HEALTH AND THE ENVIRONMENT,
Washington, DC.

The subcommittee met, pursuant to notice, at 9:58 a.m., in room 2123, Rayburn House Office Building, Hon. Henry A. Waxman (chairman) presiding.

Mr. WAXMAN. The meeting of the subcommittee will come to order.

Just over 1 month ago, this subcommittee heard remarkable testimony from the leaders of our Nation's largest tobacco companies. Testifying under oath, they told us they believe that nicotine in tobacco is not addictive, that tobacco doesn't cause disease, and advertising doesn't encourage children to smoke. In stark contrast to the findings of the Surgeon General, tobacco company executives argued that tobacco is simply one of many health risks encountered in everyday life.

Two weeks ago, we heard testimony from two Philip Morris researchers whose innovative but secret work could have alerted public health officials in 1982 to the addictive nature of nicotine. More recently, news reports have revealed evidence that knowledge of the addictive nature of nicotine was well known within the tobacco industry 20 years before Drs. DeNoble and Mele began their work for Philip Morris.

This morning's hearing is a continuation of the subcommittee's investigation of the tobacco industry. We are trying to answer a difficult question: Did the tobacco companies implement one of the most concerted and well organized conspiracies of silence in corporate America?

In a 1992 opinion involving the Liggett Tobacco Group, Federal Judge H. Lee Sarokin testified that the tobacco industry may be the "king of concealment and disinformation".

Recent reports in the media suggest that Judge Sarokin was correct. Despite industry assurances to the contrary, it now appears that a voluminous body of nicotine research was conducted over 30 years ago by the British-American Tobacco Company in England and shared with the U.S. tobacco industry through BAT's subsidiary, the Brown and Williamson Tobacco Company of Louisville, Ky.

Reports in the New York Times, Wall Street Journal, Washington Post, and other news outlets suggest that the adverse health effects of tobacco, including the addictive nature of nicotine, were by the early 1960's known and accepted by senior company officials

at Brown and Williamson. According to an account in the New York Times, these research findings so shocked the industry that a decision was made in 1963 to withhold this information from the Surgeon General's Advisory Committee on Smoking and Health. Had this information been made available, a growing number of public health authorities believe public policy toward tobacco may have been dramatically altered.

On May 11, the subcommittee invited Mr. Thomas Sandefur, Jr., of Brown and Williamson and Patrick Sheehy of British-American Tobacco to testify concerning these serious allegations. Mr. Sheehy of BAT notified the subcommittee by letter that the company would not appear to answer questions on this matter. At the request of Mr. Sandefur's attorney, we have agreed to postpone his testimony until Friday, May 20.

In light of this postponement, we will hear from only one witness this morning. Joseph Califano is currently the director of the Center on Addiction and Substance Abuse at Columbia University. As domestic policy advisor to President Lyndon Johnson and Secretary of Health, Education, and Welfare under President Jimmy Carter, Mr. Califano is uniquely qualified to comment on the impact of the tobacco industry suppression of research during the critical, formative years of U.S. tobacco control policy.

During congressional hearings in 1965, Congress heard tobacco industry scientists repeatedly criticize the findings of the Surgeon General's 1964 report. They argued that any effort to link cigarette smoking to human illness or mortality was, quote, "a considerable element of guess and gamble", end quote. But the 89th Congress didn't hear from those who conducted or evaluated the tobacco industry's secret research projects. The Congress didn't have the 1963 memorandum referred to in the New York Times where Addison Yeaman, the general counsel of Brown and Williamson, acknowledged that cigarette smoking was addictive, an admission more sweeping and clear than the findings of the Surgeon General.

Mr. Califano will testify on the impact withholding the information had on Federal efforts to curtail tobacco use and the cost to the Medicare program. In fact, the Center on Addiction and Substance Abuse at Columbia University has concluded that cigarette smoking is the largest single drain on the Medicare trust fund. Unless Congress recognizes this fact, the high cost of cigarette smoking will continue to threaten the Medicare system and will cause the expenditures of untold billions of health care dollars.

Before recognizing other members of the subcommittee for their statements, I want to make some brief comments about our hearing for next Friday. We expect the chief executive officer of Brown and Williamson, Thomas Sandefur, to testify before this subcommittee.

The tobacco industry may not like it, but their days of secrets on health research and health impacts are over. The public has a right to know this information, and this subcommittee will not be intimidated by the industry's cadre of lawyers and public relations specialists. In meeting our responsibility, this subcommittee will proceed fairly and protect the rights of every witness who testifies.

Mr. Sandefur's lawyers have made a clearly inappropriate request to review documents the subcommittee has received in the

course of its investigation. In a letter yesterday, however, which I am releasing today, I agreed to a special accommodation to address Mr. Sandefur's concerns. In Friday's hearing, the subcommittee will limit the subject matter of the hearing to Mr. Sandefur's previous testimony before the subcommittee, to documents he voluntarily provides this subcommittee, and to information provided in recent news reports.

Brown and Williamson and other tobacco executives will receive fair treatment by this subcommittee, but they will not receive special treatment.

I want to recognize other members of the subcommittee for comments they wish to make and call on Mr. Bliley first.

Mr. BLILEY. Mr. Chairman, I wish to join you in welcoming Mr. Califano to this subcommittee. I am always pleased to hear from former Cabinet officials about their work in other administrations. I know that being an administration official is often a thankless task. Individuals who take on these positions deserve our thanks for their years of public service, and I think we can all benefit from the insights former officials can bring us after they leave office.

Mr. Califano, today you are providing the committee a study which purports to show the cost of substance abuse to the Medicare program. If one turns to the methods section of your report, it is clear that the key factor determining your estimates is the estimate of the relative risk factor for acquiring a given disease.

Clearly, the relative risk factor presented in terms of a percentage is the foundation of your entire study. The important question then is, how did you determine the risk factors for a given disease or condition?

Here is what you say on pages 12 and 13 of your May 1994 report in the methods section. "When possible we selected studies that were targeted at the elderly population. However, we found that the elderly population is not often the focus of medical or epidemiological research. In lieu of elderly specific relative risks, we use relative risks for the general adult population."

My understanding of this statement is that very little epidemiologic data exists on the effects of tobacco, alcohol, or drugs on the elderly population, of those 65 years and older. Therefore, you calculated your risk factors on studies which were based on the general population.

Let's look at an example, coronary artery disease. This disease affects many of the elderly for multiple reasons, many of them centering on diet. However, in your study you attribute 64 percent of all coronary artery disease to substance abuse. Possibly this risk factor was calculated from a study of individuals much younger, say from 25 to 45 years of age, and among this age cohort this may be an accurate estimate of the risk of substance abuse for coronary artery disease. However, to then take this number and generalize it to the elderly population makes no sense.

If one looks at the elderly population, it is possible that 64 percent of coronary artery disease is attributed to high fat diets. Therefore, Mr. Califano, I want you to please make available to this committee the specific studies on which each of your risk assessments on pages 17-20 are based. Additionally, I want an age

cohort tabulation for each of these risk factors. This will help us and the press to determine the validity of your study.

Thank you, Mr. Chairman.

Mr. WAXMAN. Thank you Mr. Bliley.

Mr. Wyden.

Mr. WYDEN. Thank you very much, Mr. Chairman. I want to commend you for calling this session today and particularly to have former Secretary Califano.

I think this subcommittee in recent months has taken a special look, Mr. Califano, at the ramifications of smoking for children, and I have shared Chairman Waxman's views that is exceptionally important because we know that a substantial number of smokers are hooked before they are age 18.

But I think that you, with this new study, are making a very important contribution by turning the debate over smoking as it relates to senior citizens and to Medicare.

I think you and I have talked about it before, but I was, at home, the codirector of the Gray Panthers for a number of years before I was elected to the Congress, and I have to tell you, in my view, one of the saddest aspects of American life is to see senior citizens suffer as a result of smoking and to see all these problems of emphysema and heart disease and the like, and I think the contribution that you are making with this report has at the bottom line the basic kind of proposition that if you want to protect the Medicare program, you ought to try to discourage smoking, and I think that is an important contribution and look forward to your analysis today.

Mr. Chairman, one additional comment, if I might, with respect to the tobacco executives who will be coming on Friday. It seems to me that if those tobacco executives had reason to know that nicotine was addictive and if those tobacco executives had reason to know that tobacco smoking was carcinogenic, and if those tobacco executives manipulated the law to insulate themselves from civil liability, then my view is that the American people ought to have a right to know that and they ought to have a right to know whether or not these corporate executives protected their interests and their corporate profits rather than the health of the American people.

So I think the session that you have scheduled for Friday is a very important one. It is time to lift the veil of secrecy on the tobacco industry in this country. Friday's session is a step in that direction. I look forward to our witnesses and yield back.

Mr. WAXMAN. Thank you Mr. Wyden.

Mr. McMillan.

Mr. MCMILLAN. I thank the chairman and would like to add my welcome to Mr. Califano who has given this country distinguished service, and we appreciate that.

Mr. Chairman, I know you are well aware of my particular interest in controlling excessive costs in health care. I serve on the Budget Committee and have brought up in this broad a committee, issues related to Medicare and Medicaid over a long period of time.

Entitlement spending, as we all know, has basically been driving the budget deficit for the better part of the last decade and, unless we do something, will continue to drive it for the next decade. It clearly needs our focused, careful attention.

I am particularly interested in hearing from Mr. Califano about his work on alcohol, drug, and tobacco misuse in relation to Federal spending as it may impact Medicare and Medicaid, and I am delighted that this committee is for once considering cost containment in this area rather than cost expansion, which is usually what we are engaged in. It is my conviction that we don't consider this issue enough in a very constructive sense.

Frankly, I would have expected that HEW would have long ago addressed the issue of threats to health imposed by anything, any substance, whether it is tobacco, alcohol, drugs, fat, or we could go on and on. It seems somewhat ludicrous that we are all of a sudden awakening here in 1994 and trying to find fault with others who may have had some kind of information back in 1950's that presumably we didn't have access to.

I think I first smoked in 1950. I understood perfectly well the fact that smoking might be detrimental to my health; I think everybody who smoked understood that. Perhaps you did, Mr. Chairman. I think you used to smoke. I think we also understood the fact that it was habit forming. Whether you want to call it addictive or not addictive perhaps depends upon the individual. I think we need to try to define that word more precisely and define more precisely how we apply it to a whole array of substances.

But for you to sit here and try to suggest that your decisions not to act were because one company or one group of executives had access to information that the public didn't have access to back in the past that they conspired to withhold from the American people is absurd. I think we all understand to some degree what the risks are here, and I am perfectly willing to look at them, and I think perhaps the industry is as well.

I didn't receive the study that Mr. Califano was a part of until yesterday and haven't had a chance to examine it in detail. The first I heard of it was on the news media this morning, when it was ballyhooed as to what number of deaths tobacco contributed to among the Medicare population, which is a bottom line sound bite kind of conclusion, which is exactly what was intended.

I don't think this informs the public, it doesn't inform senior citizens, it doesn't inform me, and I think we need to be taking a real careful look at that because we run the risk of perhaps deluding the senior population into thinking that if they only deal with tobacco and alcohol, that they are going to avoid the Grim Reaper. That clearly is not the case.

On a personal note, my mother, who was a smoker, passed away of heart failure last summer. She smoked most of her life. Did she pass away because of smoking or not? She was 1 month short of 90.

You know, I think we need to—and I am as seriously concerned about the facts here as anybody else, but what this committee can do as a favor to the American people is to focus on facts instead of perception, and I hope, Mr. Califano, that you will help us do that this morning.

Thank you.

Mr. WAXMAN. Thank you, Mr. McMillan.

Well, we are here to focus on facts, not perceptions and not anecdotes, and that is why we are pleased to have Mr. Califano as a

witness to give us the results of a study of the Center on Addiction and Substance Abuse which Mr. Califano chairs.

I am pleased to have you here again before our subcommittee.

Mr. Califano was Secretary of Health, Education, and Welfare. In 1979, he issued the most comprehensive report on the adverse health effects of tobacco published to that date, and he noted the fact that there was a shocking increase in smoking among children and young teens.

Today Mr. Califano is here to tell us about the concern for another generation, the seniors who are under the Medicare program.

Mr. Califano, as is our custom in these tobacco control hearings, we would like to swear in all witnesses, and I want to inform you that at the desk there are the applicable rules, or should be the applicable rules, of the House and of this committee which informs you of the limits of the power of this subcommittee and the extent of your rights during your appearance.

Do you or any of those accompanying you have any desire to be represented by counsel or advised by counsel during your appearance here today?

Mr. CALIFANO. No, Mr. Chairman.

Mr. WAXMAN. OK. Do you or any of those who are with you object to appearing before this subcommittee under oath?

Mr. CALIFANO. No, Mr. Chairman.

Mr. WAXMAN. OK. If you have no objection to appearing under oath, I would like you to stand and raise your hand.

[Witness sworn.]

Mr. WAXMAN. Please consider yourself to be under oath, identify yourself for the record, and then we would like to have you proceed with your testimony.

TESTIMONY OF JOSEPH A. CALIFANO, JR., PRESIDENT, CENTER ON ADDICTION AND SUBSTANCE ABUSE, COLUMBIA UNIVERSITY

Mr. CALIFANO. Mr. Chairman, if I may just—there was one phrase that was left out of the statement, just for those who have it, on page 5 in the second full paragraph where the sentence should read: "The word 'addiction' does not appear in the first Surgeon General's report, except to be rejected in connection with smoking."

Mr. Chairman, my name is Joseph Anthony Califano, Jr. I am president and chairman of the Center on Addiction and Substance Abuse at Columbia University. This is my full-time occupation. I gave up the practice of law about 2½ years ago to pursue this.

Mr. Chairman and members of the committee, it is a privilege to be invited to testify before you this morning. I was Secretary of Health, Education, and Welfare when you became chair of this subcommittee. I admired and respected your work and the work of this committee, all of you—Congressman Wyden and others—then, and I have ever since.

As I said, I am now full-time chairman and president of the Center on Addiction and Substance Abuse at Columbia University. I was Secretary of HEW under President Jimmy Carter and President Lyndon Johnson's assistant for domestic affairs.

The Center on Addiction and Substance Abuse at Columbia is the only national organization to bring under one roof all professional disciplines needed to study and combat all types of substance abuse—illegal drugs, alcohol, pills, and tobacco—in all sectors of society. Our mission is to inform the American people of the costs of substance abuse throughout society and the impact on their lives, to find out what works in prevention and treatment, and to encourage all individuals and institutions to take more responsibility to combat substance abuse.

You have asked me to testify, Mr. Chairman, about how the conduct of tobacco companies which has been disclosed in recent news reports and in the New York Times—news reports in the New York Times and the Washington Post has affected Government policy over the past 30 years.

Mr. Chairman, I have been in public life for most of the past 35 years. I have been picketed, I have been attacked for one position on one issue or another, but I have never been subjected to such a crude attempt at intimidation as I was last night. At about 5 p.m. last evening there was delivered to my office at CASA the following faxed letter: "To the Honorable Joseph Califano, Center on Addiction and Substance Abuse, re: May 17 hearing of the House Subcommittee on Health and the Environment.

"Dear Mr. Secretary, King & Spalding represents Brown and Williamson Tobacco Corporation. We understand that you will participate tomorrow in a hearing of the House Subcommittee on Health and the Environment that may include a discussion of one or more articles appearing recently in the New York Times. Those articles included references to documents believed to have been stolen and which are subject to a State court injunction. A copy of that injunction is being provided with this letter." And it enclosed a copy of an injunction which purports to block anybody from talking about these documents.

Mr. Chairman, this is a blatant attempt to intimidate me, to obstruct the work of this committee, and to scare me off of testifying. I will not be intimidated, and I will lay out the facts based on those news reports, which is the only knowledge I have of their activities.

I would like to submit this for the record, Mr. Chairman.

Mr. WAXMAN. Without objection, we will receive that document for the record.

Mr. CALIFANO. For 2 years the Center on Addiction and Substance Abuse has been conducting an analysis of the cost of substance abuse to the health care system, the entire health care system. This is the first undertaking of its kind.

As the initial phase of this analysis, last year we completed and published a study of the costs of substance abuse to the Medicaid program. I have provided copies of the study to the committee and ask that the Medicaid study be entered into the record.

Mr. WAXMAN. Without objection, that will be the order.

Mr. CALIFANO. The Center's study found that at least $1 in every $5 that Medicaid spends on inpatient hospital care can be traced to substance abuse. That is at least $7.4 billion in 1994, and 40 percent of that amount, about $3 billion, is attributable to tobacco use. On average, Medicaid patients with a substance abuse as a secondary diagnosis are hospitalized twice as long as those patients

who have the same primary diagnosis but do not have a substance abuse problem.

This week the Center on Addiction and Substance Abuse at Columbia University is releasing the first study of the costs of substance abuse to the Medicare program. I have provided copies of the study to the committee and ask that it be entered in the record.

Mr. WAXMAN. Without objection, that will be the order.

Mr. CALIFANO. The study found that nearly $1 out of every $4 of Medicare spent on inpatient hospital care is attributable to substance abuse, $20 billion in fiscal 1994. This study is based on the epidemiological medical evidence, 321 footnotes cited in the material backing up this, Mr. Bliley, and also on the inpatient hospital records of Medicare which are available throughout—for the year 1991; 80 percent of that amount—80 percent of that $20 billion—is due to the long-term effects of smoking cigarettes, including lung cancer, strokes, heart disease, and respiratory ailments. The risk factors were adjusted to avoid taking into account the problem of fat or what-have-you.

And, finally, I would note that for the study we had an advisory committee which included some extraordinary people like Dorothy Rice, probably the greatest health statistician in the United States of America.

Over the next 20 years, substance abuse and addiction will cost the Medicare trust fund more than $1 trillion for inpatient hospital care. Smoking is the largest single drain on the Medicare trust fund, poised to take $800 billion over the next 20 years.

The April 11, 1994, report by the trustees of Medicare warn that Medicare will run out of money in 7 years. During that time, $128 billion of Medicare inpatient hospital costs will be due to cigarettes.

The prevalence of smoking among Medicare recipients is high. More than 36 percent of Medicare recipients are former smokers, and nearly 20 percent currently smoke. Three out of five current smokers, about 58 percent, and one-third of the quitters smoked more than 10 cigarettes a day for more than 35 years.

This puts the Medicare population at much higher risk of getting smoking-related diseases because people over 65 who have smoked tend to have done so more heavily and for longer periods of time than younger Americans.

The high prevalence of smoking among the elderly is especially disturbing in light of the documents reported in the New York Times and the Washington Post over the past several days. These reports revealed that in the early 1960's the cigarette companies knew that nicotine was addictive and that smoking caused cancer and heart disease but kept their knowledge secret in order to sell their products.

Had the American people known 30 years ago what the tobacco companies kept from them about the deadly and addictive nature of cigarettes, hundreds of thousands of premature deaths and billions in related health care costs among today's elderly population could have been avoided and billions of taxpayer dollars could have been saved.

The evasions, lies, and transfer of documents overseas by the tobacco industry to prevent any Government agency or cigarette-in-

jured patient from finding them has distorted U.S. Government policy for 30 years.

On January 11, 1964, Dr. Luther Terry issued the first Surgeon General's report on smoking and health. In his report, Dr. Terry and his distinguished advisory committee concluded that, "Cigarette smoking is causally related to lung cancer in men", but found the data for women less extensive though it pointed in the same direction.

The report also concluded that, "a relationship exists between cigarette smoking and emphysema, but it has not been established that the relationship is caused." As for that disease, the 1964 Surgeon General's report said that, "a causal relationship has not been established." The report could only associate higher mortality of cigarette smokers with many cardiovascular diseases.

The word "addiction" does not appear in the first Surgeon General's report except to be rejected in connection with smoking. Instead, the report says, and I quote, "The habitual use of tobacco is related primarily to psychological and social drives reinforced and perpetuated by the pharmacological actions of nicotine."

Mr. Chairman and members of the committee, compare what the tobacco companies knew about cigarettes and nicotine at the very time Dr. Terry and his committee were preparing the first Surgeon General's report.

On July 17, 1963, 6 months before Dr. Terry issued his report, one Brown and Williamson executive wrote—and I quote "We are, then, in the business of selling nicotine, an addictive drug."

The industry also had far more evidence of the health hazards of cigarettes with respect to cancer, respiratory ailments, and heart disease which it consciously decided not to share with the Surgeon General in order to preserve its profits. Instead, tobacco company executives chose to launch a big lie public relations and lobbying campaign to dispute what they knew to be true. What was the result?

In 1965 I was working on the White House staff of President Lyndon Johnson. The administration was pressing to put warning labels on cigarettes. The tobacco industry wanted no labeling or labeling as weak as possible. The law which Congress passed in 1965 provided only that packages of cigarettes carry labels saying, "Cigarette smoking may be hazardous to your health."

That relatively weak admonition was not changed until 1970 and again in 1984 as evidence of the dangers of smoking accumulated and thanks to the work of this subcommittee, I might note. It was not until 1972 that the Federal Trade Commission was able to extend the warning to cigarette advertising as well as packaging. Had the administration and the Congress known what the tobacco industry knew, the warnings in the health public health program of the U.S. Government would have been much stronger.

In December 1966 when President Johnson and I were discussing his State of the Union Speech, I suggested that he recommend legislation to require tobacco companies to reveal the tar and nicotine content of cigarettes in their packaging and advertising. The Department of Health, Education, and Welfare and the Federal Trade Commission wanted the President to propose such legislation.

Johnson had always been reluctant to move aggressively on cigarettes and often remarked how hard he had found it to quit smoking after his heart attack in 1954. Perpetually at odds with the south because of desegregation, he didn't want to make his political life any more difficult in tobacco-growing States.

As I pressed my case, I lit a cigarette from one of the two to four packs I smoked each day. Johnson pointed his finger at me and chuckled confidently, "The day you quit smoking those things, I'll send your bill to Congress." I didn't quit smoking until October 1975, and Johnson never sent the bill to the Congress.

The suppression of scientific knowledge that cigarettes were addictive had its most profound effect on Government public health policy during the Carter administration when I was Secretary of Health, Education, and Welfare.

Mr. Chairman and members of the committee, I have over the weekend discussed the following testimony with President Jimmy Carter and with Dr. Julius Richmond who was Surgeon General of the United States when I was Secretary of HEW.

President Carter had instructed me, as Secretary, that he wished to mount a major public health promotion and disease prevention campaign. Every physician and public health official whom I consulted said that any serious health promotion effort had to target smoking. I decided that the time had come for a second Surgeon General's report to assemble all the research of the intervening years and lay it out before the American people and the Congress.

On January 11, 1979, the 15th anniversary of Dr. Terry's first report, we issued ours. Dr. Richmond and I were able to state that the evidence that cigarette smoking caused lung cancer, heart disease, and numerous respiratory ailments like emphysema was—and I quote—overwhelming. This changed the nature of the dialogue on cigarette smoking and eventually led to strengthening labels on cigarette packaging and advertising.

What has never been revealed is the debate we had in 1978 and 1979 over whether cigarettes were addictive. Dr. William Pollin whom I had appointed as director of the National Institute of Drug Abuse, had urged the Surgeon General to declare cigarettes addictive. I also wanted Dr. Richmond to do so, but Dr. Richmond felt that we did not have sufficient data to make that finding. Since we knew that the tobacco interests would attack any report we issued, we believed it was imperative that we be on unimpeachable ground in all we said. I therefore agreed with Dr. Richmond, and we decided not to declare that cigarettes were addictive.

In discussions this weekend with President Carter and Dr. Richmond, we all agreed to this. Had we known what the tobacco companies knew and had we been privy to their research on the addictive nature of nicotine and their ability to manipulate the amount of nicotine in cigarettes, the 1979 Surgeon General's report would have found cigarettes addictive and we would have moved to regulate them. Unfortunately, the President of the United States, the Secretary of Health, Education, and Welfare, and the Surgeon General of the United States were all victims of the concealment and disinformation campaign of the tobacco companies.

It was not until May 16, 1988, almost 10 years later, that Surgeon General C. Everett Koop was able to state unequivocally that

cigarettes and other forms of tobacco "are addicting"; nicotine is "the drug in tobacco that causes addiction" and "the pharmacologic and behavioral processes that determine tobacco addiction are similar to those that determine addiction to such drugs as heroin and cocaine."

Another impact of the industry's suppression campaign on Government policy relates to research on a less hazardous cigarette. I use the term "less hazardous", Mr. Chairman, rather than the industry's term "safer cigarette" because the only safe cigarette is one that is not lit.

In August 1978, President Carter spoke of the possibility of a safer cigarette. He was concerned about the tobacco farmers at that time. Based on the advice of Dr. Richmond, I told the President that there was no such thing as a safer cigarette, that what little research had been done seemed to be going nowhere, and the talk of one would undermine the public health.

The National Institutes of Health had funded some outside research on reducing the hazards of cigarettes under the direction of Dr. Gio Batta Gori. That research was not promising, and Dr. Richmond and I decided not to pursue it. Had we known what the tobacco companies knew at the time, we would undoubtedly have conducted additional research to see if there was any possibility of producing a less hazardous cigarette. To this day, however, Dr. Richmond reminds me that our scientific knowledge suggests that as long as cigarettes contain tobacco there is no such thing as a safe cigarette.

Thus, in two respects the tobacco companies' disinformation and concealment campaign distorted the policy of the Carter administration. First, they were able to avoid any attempt to regulate them by hiding the research they had on the addictive nature of nicotine; and, second, they led us to commit fewer resources to researching the possibility of a less hazardous cigarette.

The success of the anti-smoking campaign after the second Surgeon General's report is evidence that knowledge about the dangers of smoking affects the smoking habits of America. In the 13 years from 1965 to 1978, the portion of the population that smoked fell from 40 percent to 34 percent, a decline of 6 percentage points. In the 13 years since 1978 and the release of the second Surgeon General's report in 1979, the portion of the population that smoked fell from 34 percent to 25 percent, a decline of 9 percentage points, a 50 percent greater drop.

If our message had not been diluted by the big lie advertising of the tobacco companies in their effort to portray smoking as chic and healthy, we have every reason to believe that the drop in cigarette smoking would have been much faster beginning in 1964.

Perhaps most disturbing, by deciding to conceal and deny the deadly consequences and addictive nature of smoking, tobacco companies brought—tobacco companies bought the time to scrounge for new markets. They chose two targets that were particularly vulnerable to the advertising pitch of cigarettes, women and minorities.

According to a report in Vogue magazine, in the 1960's, the tobacco industry placed 90 percent of its magazine ads in publications aimed mainly at men. By the late 1970's the industry was running half its ads in women's magazines. It paid off for them.

From 1965 to 1977 the portion of men who smoke fell from 50 percent to 41 percent, but the portion of women who smoke barely moved, from 32 percent to 31 percent. During the same period, the smoking rate among whites fell from 40 percent to 35 percent, but among blacks, African Americans, it barely budged, from 43 percent to 42 percent. Today roughly 29 percent of the black population smokes, compared to only 25 percent of whites and lung cancer has surpassed breast cancer as the leading cancer killer of women in the United States.

Tobacco is history's number one serial killer. Tobacco counts among its victims some 9 million Americans who died from smoking-related diseases between 1964 and 1994, the 30 years of concealment and disinformation.

This year, cigarettes will kill another 430,000 individuals. Cancer and heart disease victims of cigarette smoking fill intensive care units and hospital beds across the Nation. Some 54 million Americans are addicted to cigarettes, and another 8 million are hooked on smokeless tobacco. Today's tobacco users are tomorrow's carnage.

You have asked the Center to help you quantify the cost to Medicare that could have been avoided had the tobacco companies released their own research in 1963 and publicly warned Americans about the health consequences of smoking and the addictive nature of nicotine.

From 1965 to 1993, we estimate that Medicare spent $128 billion on hospital inpatient care related to tobacco use. If 10 percent fewer people were smoking during those years, Medicare could have saved $13 billion.

Looking forward, a 10 percent reduction in the number of Americans who smoked could save $80 billion in Medicare hospital costs over the next 20 years. While precise predictions are speculative, Mr. Chairman, what we can say with certainty is that if we had known then what we know now, we could have saved billions of dollars in Medicare spending alone and we could have averted millions of premature deaths and disabilities.

Today the case for increasing the excise tax on cigarettes and for FDA regulation of tobacco is overwhelming. Congress should raise the cigarette tax by at least $2 a pack. That would cut the number of smokers by almost 8 million people and over time save almost 2 million lives.

A $2 tax would raise at least $20 billion a year in revenues. Some estimates run much higher. This would compensate the American taxpayer who is paying a $19 billion tax that the tobacco companies and tobacco use imposes on Medicare and Medicaid.

The higher price of cigarettes would be most effective in deterring children from smoking. Children are especially vulnerable to the lure of cigarettes and the slick advertising of the tobacco companies. As the Surgeon General recently confirmed and as Congressman Wyden noted, virtually no one starts smoking after they are 21 years of age and for too many teenagers cigarettes are a drug of entry to the world of hard drugs.

Using data derived from the National Institute of Drug Abuse National Household Survey on Drug Abuse, the widest survey in the country, the Center on Addiction and Substance Abuse has

shown the link between cigarette smoking by 12- to 17-year-olds and the use of hard drugs. Our analysis, which you will find as attachment A to my testimony, reveals that 12- to 17-year-olds who smoke cigarettes are 12 times more likely to use heroin than those who have never used cigarettes, 51 times more likely to use cocaine, 57 times more likely to use crack, and 23 times more likely to use marijuana.

[The analysis referred to follows:]

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ATTACHMENT A

Probability of Using Drugs for Smokers and Non-Smokers (Ages 12-17)

Drug Use	Never Smoked	All Smokers		Heavy Smokers***	
	% *	%	Relative Risk**	%	Relative Risk
Any Illicit Substance	7.2	67.7	9.4	78.9	11.0
Heroin	0.1	1.2	12.0	5.1	51.0
Cocaine	0.3	15.4	51.3	31.7	105.7
Crack	0.1	5.7	57.0	11.1	111.0
Marijuana	2.5	57.5	23.0	68.2	27.3

* % of those using a given substance.

** Relative Risk is the increased probability of using the substance compared with those who never smoked. For example, a relative risk of 12 means that the smoker is 12 times more likely to use heroin than someone who has never used cigarettes.

*** Heavy smokers are individuals who smoke more than one pack a day.

All data derived from National Institute of Drug Abuse (NIDA) National Household Survey on Druge Abuse, 1991.

[For additional information contact Jeffrey C. Merrill, Vice President and Director of Policy Research and Analysis, 212-841-5240.]

Mr. CALIFANO. Raising the tax on cigarettes would put cigarettes beyond the means and lunch money of most elementary and high school students. The fact that just about everyone who smokes gets hooked as a teen and that so many of them move on to hard drugs makes this higher tax not only an immediate revenue raiser but an essential public health initiative to protect our children from being abused by tobacco companies and to prevent them from becoming a burden that will threaten the financial viability of Medicare and Medicaid.

Congress should seek to examine the research conducted by tobacco companies on their marketing strategies regarding teenagers, women, and minorities. Cigarette executives claim they do not try to target children with their ads, but in view of their concealment of the deadly diseases that cigarettes cause and the addictive nature of nicotine, it is imperative to study their market research on children as well as on women and minorities.

Congress should also withhold any Federal funds in the form of Medicare and Medicaid reimbursement from outlets that sell cigarettes such as hospitals, nursing homes, and pharmacies. Congress should outlaw cigarette vending machines and ban the advertising and sale of cigarettes within 10 blocks of any school.

These are only a few ideas, Mr. Chairman; there are many more. If we had known in 1964 what we know now, we could have turned our best minds and energy then to arresting this killer. Now, 30 years and 9 million deaths later, we must move aggressively to stop the carnage.

Mr. Chairman and members of this committee, let me close on a personal note. For most of my professional life I have been trained as a lawyer. I have been disturbed to read reports of lawyers advising their clients to move research overseas, to suppress the results and even stop the research, all because of their interest in winning lawsuits filed by people suffering from heart disease, cancer, and emphysema due to smoking. These lawyers see the end of reducing their clients' vulnerability to litigation as justifying any means, actions that they know will contribute to the disease and death of millions of Americans.

This raises profound questions about professional ethics and standards of conduct, and I hope my own profession will, in policing and examining itself, investigate the conduct of its members. But, unfortunately, we cannot rely on the better angels in tobacco executives and their hired lawyers to protect Americans from the deadly threat that tobacco poses to their health. It is up to each one of us to bar the doors and bolt the locks that will safeguard every family and child from America's number one serial killer, tobacco.

Thank you, Mr. Chairman.

[Testimony resumes on p. 290.]

[The attachments to Mr. Califano's prepared statement follow:]

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WASHINGTON, DC 20006

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FROM: Theodore M. Hester ATTY NO: 178

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DATE: May 16, 1994 NO. OF PAGES, INCLUDING COVER: 11

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May 16, 1994

Via Facsimile 212-956-8020

The Honorable Joseph A. Califano, Jr.
Center on Addiction and Substance
Abuse at Columbia University
152 West 57th Street
New York, New York 10019

Re: May 17 hearing of the House Subcommittee on Health and the Environment

Dear Mr. Secretary:

King & Spalding represents Brown & Williamson Tobacco Corporation. We understand that you will participate tomorrow in a hearing of the House Subcommittee on Health and the Environment that may include a discussion of one or more articles appearing recently in The New York Times. Those articles included references to documents believed to have been stolen and which are subject to a state court injunction. A copy of that injunction is being provided to you with this letter.

Sincerely,

Theodore M. Hester

NO. 93CI04806 JEFFERSON CIRCUIT COURT

DIVISION TEN

ROBERT L. MADDOX, ET AL. PLAINTIFFS

VS. ORDER

UNKNOWN DEFENDANT BY HIS ATTORNEY J. FOX DEMOISEY DEFENDANT

• • • • • • • • • •

Before the Court is the Plaintiff's, Wyatt, and Intervening Plaintiff's, Brown & Williamson Tobacco Corp. ("B & W") Motion for a Temporary Injunction and the simultaneous motion by the Defendant, Merrell Williams ("Williams") To Dissolve the Present Restraining Order. Both parties have filed extensive briefs and written arguments supporting their respective positions as well as responding to the opposing parties motions. The Plaintiffs also filed a reply brief to the Defendant's motion and response memorandum. Having reviewed those memorandum as well as having considered the oral arguments heard by the Court on September 29, 1993, and having reviewed the deposition of the Defendant Williams, the Court makes the following Findings of Fact and Conclusions of Law, pursuant to CR 52.01 and 65.04.

The Defendant Williams was employed as a paralegal in the Plaintiff Wyatt law firm from January 6, 1988, to some period prior to July 1993. There exist within the Plaintiff's firm an analysis project for the Intervening Plaintiff B & W. Williams was assigned to this project (affidavits of Ernest Clements, Susan Mays, Lorraine Harrison, and Barbara Boiasky).

As a result of his employment, the Defendant was required to sign a nondisclosure agreement similar to one attached to the original complaint on Exhibit 2, or Exhibit B attached to the Plaintiff's Motion for Temporary Injunction (these are similar, but different forms). The

Defendant denies recognizing either document as one he has ever signed (Defendant deposition page 14, line 22). Both forms were shown to him during his deposition. The Defendant goes on to say that he may or may not have signed a similar document (deposition page 15, line 4). The Defendant's counsel raises the question of where is the original signed contract. However, in a letter to the Plaintiff dated July 9, 1993, counsel admits to having reviewed the subject employment contract and acting in accordance with that contract advised the Defendant to return the documents to the Plaintiff (Exhibit D to Defendant's Brief to Disolve the Restraining Order). The Court believes, based on the exhibits and the Defendant's evasive answer that the contract exists and a copy is in the Defendant's possession. Paragraph Three, in both forms, clearly indicates an employee, upon termination, will not remove any confidential information, reproduction or personally made records and will immediately return any such records already removed (emphasis added). Counsel for the Defendant erroneously concludes this paragraph is limited to material taken at the time of termination. Such a restrictive reading of this paragraph is neither logical nor workable. The logical extension of the Defendant's reasoning would require him to return only those documents in his hands when he's told he's terminated. In performance of the contract, the Defendant should have returned all documents, including self-made copies related to his employment.

The second document to have been signed by the Defendant was a "Confidentiality of Information" form expressing the Plaintiff Wyatt's firm policy (Exhibit 1 attached to the original complaint and Exhibit A as attached to the Plaintiff's Motion for a Temporary Injunction). The Defendant admits to recognizing the document (deposition page 13, line 2), but then questions whether or not the signature on the second page as his (deposition page 17 line

5 through page 18, line 13). The firm policy clearly prohibits disclosure of any matters involving clients to persons outside the firm.

During the Defendant's employment with the Plaintiff Wyatt he was permitted access to confidential matters involving the Intervening Plaintiff B & W. Apparently, while employed he made copies of documents at the firm and took them home (or may have taken the originals out of the office, copies, then returned them). The Defendant, through counsel, subsequently on July 9, 1993, notified the Plaintiff of the existence of this separate file. On advice of counsel these documents were returned. The Defendant then threatened to sue the Plaintiffs unless his claims for proposed injuries were settled.

The Plaintiffs have repeatedly referred to the Defendant as a thief and that his actions resulted in a theft of documents from the Plaintiff Wyatt. Clearly in our current age of photocopy technology and under our rules of evidence (KRE 1003 and 1004) a copy may be the equivalent of the original. The Defendant's actions could potentially fall under the purview of several statutes within the penal code including Burglary in the Third Degree (KRS 511.040) or Criminal Trespass in the First Degree (KRS 511.060) assuming he entered into the building without permission and with intent to take documents after his employment ended or at any time he did not so have permission. Other potential charges include Theft By Extortion (KRS 514.080) although it would appear there would have to be a threat of a lawsuit to accomplish a theft and not a theft and then threatening a lawsuit. The defense set out in KRS 514.080(2) is an affirmative defense which would have to be asserted after the Defendant is so charged. Another possibility includes Misapplication of Entrusted Properties (KRS 517.110).

This list of criminal charges is not meant to be exhaustive, but certainly Defendant's counsel must believe his client could be charged with a criminal offense or he would not have encouraged him repeatedly to assert his Fifth Amendment right against self-incrimination during the deposition on October 6, 1993 [It is important in this Court's final analysis to remember how the Defendant came into possession of these documents as this fact scenario is clearly distinguishable from cases cited by the Defendant in determining whether or not a crime/fraud exception to the attorney-client privilege exists. See also Supreme Court Rule 1.6 (b)].

Shortly after the return of the copied documents, the Defendant reveals that he had prepared a narrative and a sealed copy of same was provided to the Plaintiff Wyatt (September 22, 1993, letter from the Defendant's counsel to Plaintiff, attached as Exhibit G to Defendant's Brief to Dissolve the Restraining Order). The narrative quotes verbatim, documents already returned to the Plaintiff (Affidavit of J. Kendrick Wells). The Court is able to gleem from the Defendant's Brief that the narrative may include information from various sources including documents taken from the Plaintiff, information the Defendant "learned" during the course of his employment work product of non-attorney's utilized by the Plaintiffs Wyatt and Brown & Williamson i.e. accountants and information from third parties not associated with this litigation. The Defendants are concerned solely with the first three categories and as they may be protected by the attorney-client privilege.

The Plaintiff has asserted that the information taken by the Defendant whether documents or knowledge is subject to the attorney-client privilege. Although this Court recognizes that not all information within an attorney's file is subject to the privilege, it is safe

to assume that this information was confidential or else the Defendant would have been able to obtain it from a third source. Likewise, information compiled by statisticians, accountants, scientists, etc. in preparation for future litigation is also so protected.

The Defendant asserts that even if privileged, the privilege is not absolute. This Court recognizes that a long line of cases, both Kentucky and Federal decisions, as well as our own Supreme Court Rule 1.6(b) hold that the privilege does not extend to communications between attorney and client where the client's purpose is the furtherance of a future intended crime or fraud. Standard Fire Insurance Co. v. Smithhart, Ky., 211 S.W. 441 (1919); Ridener v. Commonwealth, Ky., 75 S.W.2d 737 (1934); Strong, et al. v. Abner, Ky., 105 S.W.2d 599 (1937); Clark v. U.S., 289 U.S. 1, 77 L.Ed. 993, 53 S.Ct. 465 (1933); U.S. v. Zolin, ___ U.S. ___, 105 L.Ed. 469, 109 S.Ct. 2619 (1989); Haines v. Liggett Group, Inc., 975 F.2d 81 (3rd Cir. 1992).

Before this Court can determine whether the allegedly privileged communications fall within the crime/fraud exception an in camera review would be necessary. But before even that hearing can be conducted, the Defendant Williams would have to present evidence sufficient to support a reasonable belief that an in camera review may yield evidence establishing the applicability of the crime/fraud exception. U.S. v. Zolin, 109 S.Ct., at 2630; Haines v. Liggett Group, Inc., 975 F.2d at 96. A blanket rule allowing judicial examination of the disputed documents based on bare allegations of fraud is no more favored than a blanket rule barring such review. U.S. v. Reynolds, 345 U.S. 1, 97 L.Ed. 727, 73 S.Ct. 528 (1953).

> Before engaging in in camera review to determine the applicability of the crime/fraud exception, "the judge should require a showing of a factual basis to support a good faith belief by a reasonable person" Caldwell v. District Court, 644 P.2d 26, 33 (Colo. 1982), that in camera review of the

> materials may reveal evidence to establish the claim that the crime/fraud exception applies. U.S. v. Zolin, supra at 2631.

Zolin requires the Court to make a decision in light of the facts and circumstances of the particular case. In the case at bar, the Defendant Williams has presented no facts upon which this Court can rely upon to initiate an in camera review.

Obviously the Defendant will point to the Restraining Order issued September 29, 1993, as the reason for his inability to present the Court with facts. At first blush, it would appear that this handicap is due solely to judicial action. However, the manner in which this information was obtained, i.e. by the Defendant and as this Court has already stated, in violation of the employment contract between the Plaintiff and Defendant created this "Gordian Knot," not the Court's Order.

"The threshold showing to obtain in camera review may be met by using any relevant evidence, lawfully obtained that has not been adjudicated to be privileged." U.S. v. Zolin, 109 S.Ct. at 2632 (emphasis added). By no stretch of judicial imagination can this Court find the material in question was "lawfully obtained." Whether it was obtained in violation of a contractual agreement or contrary to our penal code, this Court will not sanction such activity by agreeing to an in camera proceeding. To do so would encourage litigants to break into opposing counsel's office or administrative offices of the opposing party to seek allegedly damaging correspondence between the attorney and client. The Defendant's action in this case clearly distinguish Plaintiff's actions in Haines, where the Plaintiff learned through the Cipollone v. Liggett Group, Inc., 683 F.Supp. 1487 (D.N.J. 1988) of documents relating to her claim against Liggett Group, et al. These documents, divulged during discovery in the Cipollone case gave rise to a pretrial discovery request in the Haines case. The Judicial in camera review was clearly

proper in light of relevant, lawfully obtained non-privileged information which led the Court that an in camera review was necessary.

The Defendant having failed to show that the attorney-client privilege should be abrogated, the next question arises as to whether or not the Plaintiff and Intervening Plaintiff met the burdens under CR 65.04(1) to grant a temporary injunction and a return of all documents including the narrative. Tantamount in deciding this issue is what harm may befall the Plaintiffs, particularly the Intervening Plaintiff, B & W, if these materials are not returned.

Although the attorney-client privilege may not be sacrosanct, it is certainly a bed rock principle upon which our judicial system rests. It is clear to this Court that divulging any detrimental information (as admitted by the Defendant) subject to the attorney-client privilege would cause the Intervening Plaintiff, B & W, to suffer immediate and irreparable harm. The Defendant has violated the contract by removing documents and has clearly threatened to violate the privilege by using those documents in a lawsuit against the Plaintiff Wyatt and Intervening Plaintiff B & W. The privilege applies to the Defendant even though he was a paralegal. In re Grand Jury Subpoena Duces Tecum, 391 F.Supp. 1029 at 1034 (S.D.N.Y. 1975). Williams v. TransWorld Airlines, Inc., 588 F.Supp. 1037 at 1044 (W.D. Mo. 1984). The privilege applies not only to the documents stolen, but the knowledge garnered by the Defendant during his employment with the Plaintiff Wyatt. American Motors Corp. v. Huffstutler, 575 N.E.2d 116 (Ohio 1991). There is no way to provide monetary compensation for a disclosure of such information nor to repair the damage to society's confidence in the privilege if such a breach is permitted. Such disclosure would be detrimental to the integrity of the Plaintiff Wyatt and the

working relationship it enjoys with the Plaintiff B & W and other clients. Maupin v Stansbury, Ky.App., 575 S.W.2d 695 (1978).

Wherefore, for all the reasons stated above in the body of this Order, the Defendant's Motion for an in camera review and to dissolve the Temporary Restraining Order are **DENIED**. The Plaintiff's Motion for a Temporary Injunction is **GRANTED**, and

IT IS HEREBY ORDERED that:

1. Defendant, Merrell Williams, and his agents, attorneys, successors and assigns, and all persons participating with, or acting on his behalf or within his control or direction or in concert with him, and all persons who are informed of this Restraining Order are hereby restrained and enjoined from:

(a) Disclosing to anyone other than the Plaintiffs or Intervening Plaintiff any material or information in the possession or control of the said Defendant, Merrell Williams, including, without limitation and whether in the category of "privileged" or "confidential" or otherwise: (i) all documents, computer discs and drives and other storage/retrieval systems and other tangible and electronic materials and things belonging to Plaintiffs or any of their clients, including, without limitation, Intervening Plaintiff, B & W; (ii) all information contained therein and thereon, all information learned therefrom, and all information learned in connection with the employment of Merrell Williams by Plaintiffs or Intervening Plaintiff; and (iii) all documents, manuscripts, narratives, reproductions, copies, storage and retrieval systems and charts, graphs or tables

on which any part of (i) or (ii) in this definition has been collected, stored, portrayed, summarized, or referred to, in any manner.

(b) Using for any purpose or in any manner any of the material or information defined in paragraph 1(a) hereof; and

(c) Reproducing in any way any of the material or information defined in paragraph 1(a) hereof.

2. Defendant, Merrell Williams, and all other persons and entities bound by this Temporary Injunction are hereby directed to immediately turn over to John T. Ballantine, Ogden Newell & Welch, 1200 One Riverfront Plaza, Louisville, Kentucky 40202, all of the above-described material and information in sealed container(s); and such seal(s) shall not be broken, and the container(s) shall be stored by John T. Ballantine in such manner as the parties may agree and, failing any such agreement, shall be kept by John T. Ballantine under lock and key until further order of the Court.

3. The Plaintiff shall post a bond of $1,000.00.

SO ORDERED, at 2:15 p.m. on January 7, 1994.

THOMAS B. WINE, JUDGE

DATE: January 7, 1994

cc: John T. Ballantine
J. Fox DeMoisey
Gordon A. Smith

ENTERED IN COURT

JAN 7 1994

TONY MILLER, CLERK

By D.K. Davis
Deputy Clerk

THE COST OF SUBSTANCE ABUSE TO AMERICA'S HEALTH CARE SYSTEM

Report 1: Medicaid Hospital Costs

July 1993

I. INTRODUCTION

Health care reform has emerged as a major issue on our nation's domestic agenda. But, as the history of health system reform efforts has repeatedly demonstrated, providing quality care to all Americans at reasonable cost is no mean task. It requires an examination of all the factors that contribute to health care inflation, including administrative costs and inefficiency, inappropriate and excessive use of services, malpractice and defensive medicine, emerging technologies, and excess capacity. Eliminating unnecessary Cesarean sections may save $1 billion, eliminating unnecessary bypass surgeries may save a little more, reducing excess capacity might save several billion, but, in the hierarchy of cost containment opportunities, another cost of far greater magnitude ranks high on the list: that of reducing substance abuse and addiction in all its forms--including tobacco, alcohol and drugs.

CASA -- The Center on Addiction and Substance Abuse at Columbia University -- is conducting the first national, comprehensive study of the costs of all substance abuse -- legal and illegal drugs, alcohol, and tobacco -- to the nation's health care system. The first phase of this study, funded by the Henry J. Kaiser Family Foundation, focuses on the inpatient hospital costs of the Medicaid program. Subsequent reports will assess the costs of substance abuse to the rest of Medicaid (e.g., outpatient hospital costs, emergency room services, payments to physicians), Medicare, other public programs, Blue Cross/Blue Shield, commercial insurers, institutions and individuals.

Impact of Substance Abuse and Addiction on Health Care

Substance abuse and addiction is not confined to one illness. Its costs to the system go well beyond what is spent on direct treatment. Substance abuse is ubiquitous, reaching every corner of health care from ailments such as cancer and cardiovascular disease to trauma, birth complications and AIDS. Substance addiction and abuse is the sole cause for diseases such as alcohol cirrhosis and fetal alcohol syndrome. It is also a major risk factor for other costly health problems, including lung cancer and coronary heart disease. It complicates all sorts of otherwise unrelated diseases and ailments, such as severe burns and pneumonia, adding days and dollars to treatment.

Estimates vary about the total direct and indirect cost of substance abuse to the health care system: they run as high as $140 billion a year and, thus, represent a significant portion of the total health care bill. Whatever the cost, it is clear that achieving meaningful health care reform will be difficult without addressing the problem of substance abuse.

Substance abuse affects health care expenditures in both the long-term and the short-term. What we are seeing in health care expenditures, including Medicaid's, is the result of the cumulative effects of using and abusing substances over many years. This leads to illnesses such as heart disease and cancer. However, some costs stem from the more immediate medical effects of substance abuse -- birth complications, injuries resulting from violence and accidents, AIDS, and strokes among younger people who overdose on drugs. Reducing the longer-term costs is important, but these shorter-term costs have special relevance in the context of health care

reform, since they promise more immediate savings. While substance abuse will never be eliminated entirely, some consequences are so immediate that even gradual reductions in use will produce savings in the short term.

Medicaid and Substance Abuse

Medicaid was chosen as the initial area for analysis for a variety of reasons. First, the skyrocketing costs of the Medicaid program top the concerns of nearly every governor in our nation. The program does not provide adequate health care to poor people, yet its costs are breaking state budgets. The current crisis prompted the Henry J. Kaiser Family Foundation to create a commission to examine Medicaid and investigate ways to improve the program while containing costs.

Second, the Medicaid program covers a large number of pregnant women and children. Substance abuse has a significant impact not only on pregnancy and birth outcomes but also on life-long health care costs for infants born to substance-abusing mothers. Lastly, the growing problem and mounting costs of AIDS is disproportionately borne by the Medicaid program since it is often the payer of last resort for a population disenfranchised from the private insurance system.

In any assessment of where best to target limited resources, the impact of substance abuse on Medicaid expenditures must be considered. This study demonstrates that substance abuse takes a heavy toll on already limited Federal and state tax dollars, yet there is no explicit

reimbursement of substance abuse treatment or prevention services under Medicaid, nor are states required to offer such benefits (though some states offer limited services).

Substance abuse is not a problem only for Medicaid recipients, nor are they necessarily the most costly population in this regard. Smoking, alcohol and drug abuse are equal opportunity problems affecting all segments of our society regardless of income, race or social status. Indeed, the techniques we have developed to analyze Medicaid costs through medical and epidemiologic evidence forms the foundation for our broader study of the relationship between substance abuse and morbidity across all populations and all payers.

Background

Enacted in 1965, Medicaid was intended to take care of the medical needs of low-income individuals who were either part of families with dependent children, permanently and totally disabled, or elderly. The program is not only directed at the acute care needs of this population, but also finances long-term care for the needy elderly and chronically ill.

Unlike Medicare, which is considered social insurance and funded through a combination of payroll taxes, premiums, and general Federal revenues, Medicaid is a welfare program, with eligibility linked to the Aid to Families with Dependent Children (AFDC) and Supplemental Security Income (SSI) programs, and is funded through general revenues generated by the states and Federal government.

Medicaid is a state-administered program in which the Federal government matches state payments on a formula basis. While all states are required to meet certain federal requirements with respect to eligibility and benefits, considerable latitude is permitted in determining eligibility, the inclusion of additional benefits, and the method and level of payment for services.

In fiscal year 1994, the combined Federal and state payments under the Medicaid program are estimated to reach $146 billion. Of this, total hospital costs (including psychiatric facilities) will represent 28 percent or $41 billion. Since 1980, Medicaid costs have grown at an annual average rate of 13 percent, as opposed to only a 4.4 percent annual increase in the Consumer Price Index (CPI).

II. METHODS

Many studies have sought to estimate the cost of substance abuse, in one form or another, to society (See Chapter V). For the most part, these studies have analyzed the cost of one or two substances. None has estimated the costs of all substances to a particular insurer.

While building upon earlier work, we go beyond it in a number of ways. CASA's study quantifies in a single report the total cost of substance abuse in all its forms (tobacco, alcohol, and legal and illegal drugs). It enlarges earlier efforts to incorporate findings from epidemiologic research in health care cost analyses. Based on the best available epidemiologic studies, we have determined the proportion of patients who acquired diseases or conditions as a result of the abuse of alcohol, drugs, or tobacco. These related costs are factored into our total cost estimate. Finally, this study suggests areas for further research and for new policy directions to address the problem of substance abuse and its costs.

The following section briefly describes CASA's methodology for estimating Medicaid inpatient hospital costs related to substance abuse. A technical paper describing this methodology in more detail is being prepared for subsequent publication.

General Hospital Inpatient Costs

In order to estimate hospital costs associated with substance abuse, we have divided these costs into four general categories:

1) Direct treatment of substance abuse;

2) Treatment of medical conditions totally attributable to substance abuse;

3) Treatment of medical conditions where substance abuse is a major risk factor; and

4) Treatment for medical conditions whose length of stay was extended due to complications arising from a secondary diagnosis of substance abuse.

We calculated the costs for each category by multiplying the number of hospital days attributable to substance abuse for the diseases and conditions in each category by an average inpatient hospital cost per day. To estimate the number of Medicaid substance abuse-related days in each category, we used hospital utilization data from the 1991 National Hospital Discharge Survey (NHDS) [1] applying the following criteria:

1) Direct Treatment - If the discharge had a primary diagnosis of either substance dependence or substance-induced psychosis or poisoning, the hospital stay was assumed to be for the direct treatment of the substance abuse problem. For these diagnoses, 100% of the hospital days were attributed to substance abuse.

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[1] *The National Hospital Discharge Survey is conducted annually by the National Center for Health Statistics. It is a national sample of more than 400 short-stay hospitals, producing over 200,000 discharges annually. The data are abstracted from the patients' medical records and include demographic information, up to five diagnoses coded according to the International Classification of Disease (ICD-9-CM), surgical procedures, length of stay, and expected source of payment. The sample is weighted to derive national estimates of hospital utilization.*

2) Treatment of Diseases Totally Attributable to Substance Abuse - In Category 1, the hospital stay was specifically for the treatment of the substance abuse problem. For this and the next category, the hospital stay was for treatment of a medical disease that may have been caused by the use or abuse of a substance. In this category are discharges that had a diagnosis that either specifically mentioned a substance in its name (e.g. alcoholic cirrhosis), or that the National Institute on Alcoholism and Alcohol Abuse considers as solely attributable to alcohol (e.g. pellagra), or that involve a secondary diagnosis of substance abuse in 100% of the NHDS cases reported (e.g. esophageal varices). Since the hospital stay was for medical treatment of diseases caused solely by substance abuse, 100% of these hospital days were attributed to substance abuse.

3) Treatment of Diseases Where Substance Abuse is a Major Risk Factor - From an extensive review of epidemiologic research (see Bibliography), CASA identified 72 conditions and diseases that have substance abuse as a major, but not the exclusive risk factor. These include diseases such as lung cancer and low birth weight associated with smoking; accidents and cardiovascular diseases associated with alcohol use; and premature strokes and AIDS associated with drug use. The prospective, population-based or case control studies used for this analysis often calculated (or provided sufficient data for CASA to calculate) a Population Attributable Risk (PAR) for a specific substance and disease. PAR is an epidemiologic term meaning the percentage of a given illness that could be prevented if the use of the substance were eliminated.[2] In other words, the

[2] *These PARs are based on the best available epidemiologic research investigating the relationship between substance abuse and morbidity. For some diseases and conditions, there was clear evidence that a relationship exists between substance abuse and the occurrence of the condition, but prospective or case control studies which calculate PARs had not been conducted. In these cases, we employed other*

PAR for cigarettes and lung cancer is 87% indicating that 87% of lung cancers could have been prevented if there were no cigarette smoking. Based on extensive research, we assigned a PAR for each of the 72 substance-abuse related diseases (which are listed in the Appendix). With the help of a medical records coder, we then identified the diagnostic codes associated with these diseases. For each Medicaid discharge that involved any of these primary diagnoses, we multiplied the associated PAR for that disease by the total number of Medicaid days reported for that diagnosis to determine the days attributable to substance abuse.

Two health problems, AIDS and birth complications proved particularly difficult with respect to estimating their costs resulting from substance abuse. For example, determining AIDS days was difficult, given that an AIDS-related condition (such as pneumocystosis) is often the primary diagnosis and AIDS is only listed secondarily. In fact, only 10,000 Medicaid discharges had AIDS as the primary diagnosis, clearly an underestimate. To further complicate matters, not all cases that have AIDS as a secondary diagnosis are hospitalized due to AIDS: someone may be hospitalized for an appendicitis and only coincidentally have AIDS. Thus, these hospital days could not be attributed to AIDS or substance abuse. To get a more precise estimate of AIDS-related hospital days, we identified the primary diagnoses for all Medicaid discharges that had

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measures than PARs, including estimates from large surveys and from medical experts. For example, in the case of AIDS, we used 1992 Center for Disease Control (CDC) surveillance data to estimate the percentage of these cases that were caused by intravenous drug use (IVDU). This surveillance data does not establish causality, it merely categorizes new cases by the risk groups they fall into. In 1992, 55% of new pediatric AIDS cases, and 33% of adult cases fell into the IVDU risk group. We applied these percentages to total reported Medicaid AIDS days to estimate those that were substance abuse-related.

a secondary diagnosis of AIDS. Then, consulting with physicians specializing in AIDS care and research, we selected those primary diagnoses that are AIDS-related. These AIDS-related hospital days were added to the hospital days for patients discharged with a primary AIDS diagnosis and then multiplied by the percentage of Intravenous Drug Use (IVDU) as determined by the Center for Disease Control (CDC) AIDS Surveillance (see Footnote 1) to determine substance abuse related AIDS days.[3]

Birth complications also required special analysis. Since the abuse of a substance is not responsible for the admission (i.e., the birth itself), but only for certain associated complications, we needed to calculate the marginal impact of those complications. For alcohol, the number of incremental days was a simple calculation of the difference in the number of days where alcohol was indicated as a secondary diagnosis. With respect to the impact of smoking, a PAR was applied to low birth weight babies and the number of days was calculated as described above. However, the length of stay for a normal neonate (2.3 days for each discharge) was deducted from this since, absent the complication, this number of days still would have been used. For cocaine-exposed babies, costs related to birth complications were estimated based upon a 1986 study by Phibbs, et al of the added days associated with babies exposed to cocaine and other drugs. The results of this study (based upon a multivariate analysis) estimated that, in

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[3]A similar problem exists for other diseases such as lung cancer where, after the initial diagnosis, future hospitalizations would be for other problems or procedures such as respiratory distress or chemotherapy. However, disentangling the overlap between alternative causes for these other diagnoses and those attributable to the lung cancer made it difficult to count those days in our estimates. Thus, there is reason to believe that our estimates are low since this problem would exist for a number of diagnoses.

the case of a baby exposed to cocaine, the average length of stay was eleven (11) days longer than for one without this exposure. To estimate the incremental days attributable to drugs, the total number of Medicaid births involving maternal cocaine use (8% of all births) was multiplied by 11 days.

4) Additional Days for Medical Treatment Due to Substance Abuse Complications - In addition to being a risk factor for getting certain illnesses, active substance abuse at the time of hospitalization can also complicate an illness and add to the patient's length of stay. For example, substance abuse can compromise the immune system, reducing the body's ability to fight infection or some substance abuse problems (e.g., delirium tremens) need to be stabilized before doctors can treat the primary medical condition. To estimate the cost of substance abuse comorbidity, we computed the difference in length of stay between those discharges with the same primary diagnosis with and without substance abuse as a secondary diagnoses, controlling for age and sex. The total number of incremental days identified in this way were counted as substance abuse-related Medicaid days.[4]

For each of these four categories, we estimated 1991 costs by multiplying the identified substance abuse-related days by an average hospital inpatient per diem cost of $750. This per diem estimate was based on 1990 Medicaid costs per day inflated by the hospital component of

[4] *With respect to this fourth category, our analysis understates the impact of substance abuse comorbidity due to limitations of medical reporting (See Underestimation Issues).*

the CPI to 1991 levels.

Psychiatric Hospital Inpatient Costs

Since the National Hospital Discharge Survey only includes general hospitals, we employed a different method to estimate substance abuse-related Medicaid psychiatric hospital inpatient costs. The 1991 Survey of the National Association of Psychiatric Health Systems indicates that 11% of patients in their facilities had a primary diagnosis of alcohol or substance-related disorders. Multiplying this percentage by 1991 Medicaid expenditures on psychiatric inpatient care, we estimated that substance abuse-related illness in psychiatric hospitals accounted for $238 million in Medicaid costs in 1991.

This is a conservative estimate of substance abuse's impact on psychiatric hospitals. Psychiatric hospitals often do not list substance abuse as the primary diagnosis because many insurers will not pay for psychiatric care unless the primary diagnoses is a specific psychiatric disorder. A large percentage of the psychiatric inpatient population are dual-diagnosed with a psychiatric disorder as the primary diagnosis and a substance abuse disorder as the secondary diagnoses. The limitations of our data restricted us from estimating the costs of these clients, but anecdotally we know that the dual-diagnosed population is increasing and that these clients use a much greater percentage of psychiatric hospital staff resources.

Underestimation Issues

These estimates of the cost of substance abuse to Medicaid are likely to be lower than the actual

costs. First, while we have attempted to pull together all available epidemiologic research on the health effects of substance abuse, more research is needed. Our results only reflect the current state of the art in this area.[5] Second, studies reveal that identification and reporting of substance abuse problems by medical practitioners is poor. For example, estimates of underreporting of substance abuse secondary diagnoses run as high as 60%. For reasons of confidentiality and concern over insurance reimbursement, physicians are reluctant to record substance abuse unless it relates directly to the primary diagnosis or the treatment plan. Assuming that only 40% of cases with substance abuse actually listed it on the medical record, the complicating costs of substance abuse comorbidity may be two and a half times higher than estimated here. Third, there is little identification of tobacco use or abuse of prescription medications on the medical record: our estimates only include the complications of alcohol and illicit drug abuse. Fourth, using an average hospital cost of $750 per day may be low if substance abusers require a greater intensity of services. For example, if substance abuse burn patients are more likely to stay longer in the Intensive Care Unit (ICU) at an average cost per day of $3,000, these additional costs would not be captured in our analysis[6]. Finally, our estimates do not include general hospitalization costs of caring for people who join the Medicaid rolls, and benefit from its coverage, due to job loss, disability, or poverty, related to substance abuse.

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[5] *The association between illegal drug use and resulting illness has not been as thoroughly studied as that of smoking and alcohol because drug use is less prevalent in the general population and more difficult to identify since subjects are reluctant to admit openly to illegal conduct. Alcohol studies are also somewhat limited, due in part to the greater difficulty in establishing level of use (self-reporting of alcohol use is less reliable than that of tobacco because heavy use of alcohol has a negative social stigma). Even for cigarette smoking, a great deal of research is available on illnesses highly prevalent in the population such as lung cancer and heart disease, but less is available for less prevalent diseases, such as Crohn's disease. Thus, our study only includes those diseases and conditions that have been clearly documented as related to substance abuse. We attempted to use the best research available, recognizing that the field of epidemiology is constantly evolving and sharpening its findings. Further inquiry into other related conditions would most likely significantly increase substance abuse-related Medicaid hospitalization costs.*

[6] *A study at Johns Hopkins Hospital revealed that 28 percent of 435 ICU admissions and 39 percent of ICU costs were substance abuse-related (Baldwin et al).*

III. RESULTS

In 1991, Medicaid spent $4.2 billion, or 19.2 percent, of its $21.6 billion in inpatient hospital expenditures on substance abuse-related care. Based upon these results, it is estimated that for fiscal year 1994, substance abuse related costs would rise to $7.4 billion. The largest share of Medicaid substance abuse costs in hospitals -- $3.4 billion or 81 percent of the total costs -- was for medical treatment of substance abuse-related illnesses and conditions and for the increased length of stay required for patients with a coexisting substance abuse disorder. Treatment for obvious substance abuse disorders such as drug overdoses, delirium tremens, drug or alcohol dependence and abuse, and substance abuse psychoses in general and psychiatric hospitals accounted for $0.7 billion of the $4.2 billion.

Most surprising, our analysis of the epidemiologic evidence reveals that 72 conditions requiring hospitalization are wholly or partially attributable to substance abuse (they are listed in the Appendix). And this list is probably not complete; though we reviewed more than 3,000 articles and papers, we were limited by what epidemiologic research has been done to date.

The following charts and tables display and describe our findings in detail.

Charts 1-4

Charts 1 and 2 summarize the impact of substance abuse on Medicaid inpatient hospital utilization and costs. Charts 3 and 4 break down these results by substance and by the short and long-term savings that can be accrued as a result of reducing substance abuse.

Substance abuse-related hospital care accounted for 19.2% of total Medicaid hospital costs and 20% of total days in 1991. The reason for the discrepancy between the percentage of costs and days is that some of the days are in psychiatric hospitals which have a lower average cost per day than that of acute care, general hospitals.

Chart 3 breaks down substance abuse-related costs by the substance involved. Tobacco and illicit drugs contribute more to Medicaid hospital costs than alcohol. The unexpectedly high proportion of hospitalizations attributed to illicit drug use is due to birth complications resulting from cocaine use (Phibbs et al). Since Medicaid disproportionately serves women and children, a very large share of overall Medicaid hospitalization costs are, therefore, for births and birth complications.

The drug-related costs associated with birth complications may be somewhat overstated: while a significant portion of these costs were attributable to drugs, some may also be attributable to alcohol since many drug addicts also abuse alcohol. The high correlation between drug and alcohol use among these pregnant women makes it hard to separate out the effects or determine

which substance is the real culprit. In either case, whether as a result of alcohol or drugs, or both, the problem of adverse birth outcomes is strongly associated with substance abuse.

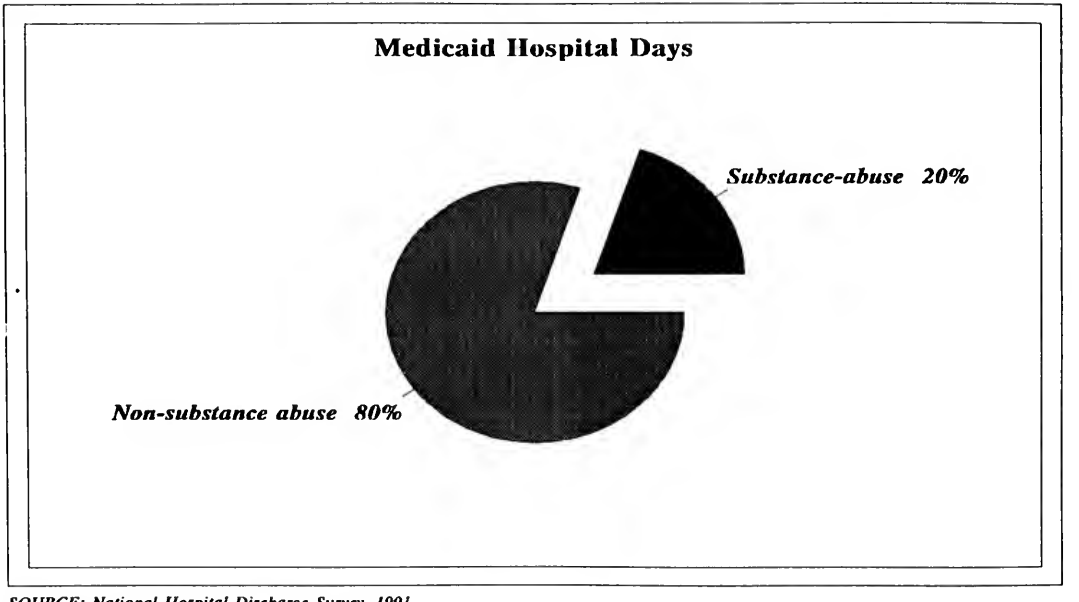
Chart 4 breaks down the short- and long-term impact of substance abuse on morbidity. The $2.93 billion total in Chart 4 does not add to the total in Chart 1, since Chart 4 includes only costs related to substance abuse as a risk factor in other conditions and does not take into account substance abuse as either a secondary diagnosis or a direct treatment cost. The reason for including this table is to note that reductions in substance abuse can have a real and immediate impact on costs. In the case of birth outcomes, trauma, AIDS, and strokes among younger people, reducing substance abuse can have a significant immediate effect on health spending. By contrast, in the case of diseases like lung cancer, where the disease is acquired through long term abuse of a substance, reducing current substance abuse will not immediately affect health care costs -- the savings would be accrued over time as less people in the future acquire those diseases.

Chart 1: Estimated 1991 Substance Abuse Impact on Medicaid Inpatient Hospital Costs

Substance Abuse-Related Costs	$4.2 billion
Total Hospital Costs	$21.6 billion
% of Total	19.2%

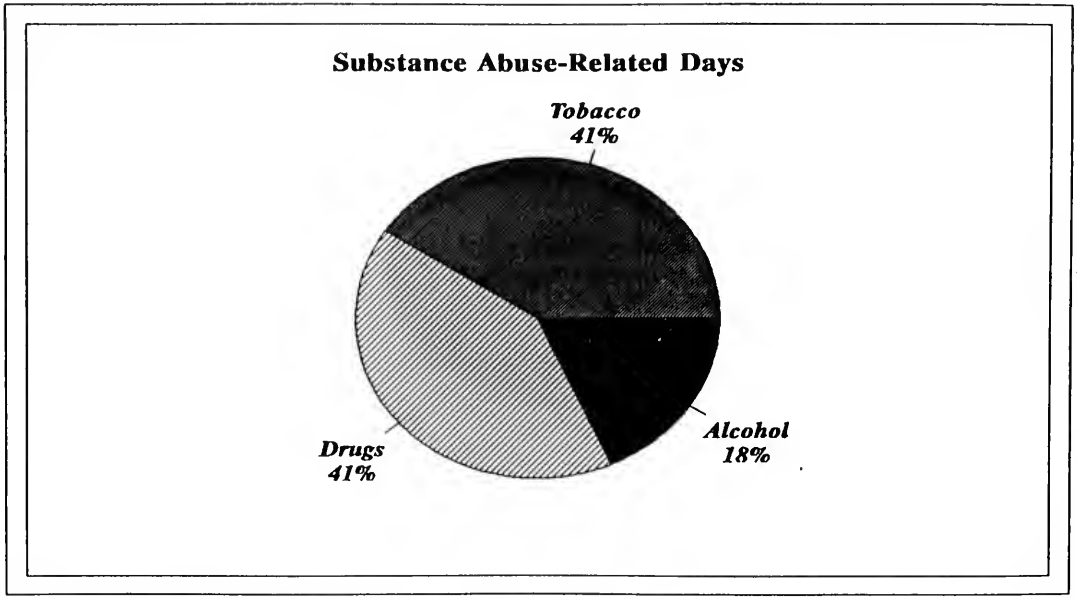
SOURCES: National Hospital Discharge Survey 1991; Health Care Financing Administration - Office of the Actuary - 1993 Medicaid Statistics

Chart 2: 1 out of 5 Medicaid Hospital Days Associated with Substance Abuse



SOURCE: National Hospital Discharge Survey, 1991.

Chart 3: Medicaid Substance Abuse-Related Hospital Days by Substance



SOURCE: National Hospital Discharge Survey, 1991.

Chart 4: Substance Abuse and Medicaid

Short and Long-Term Costs

- Short-term Costs $1.93 billion
- Long-term Costs $1.00 billion

Chart 5: Substance Abuse Costs to Medicaid

Total Hospital Care, 1991

			% of Total
1. Direct Treatment for Substance Abuse		$776,305,150	18.7
General Hospitals - Inpatient	$538,607,250		
Psychiatric Hospitals	$237,697,900		
2. Treatment for Diseases/Conditions Totally Attributable to Substance Abuse		$112,014,143	2.7
3. Treatment for Diseases/Conditions Where Substance Abuse Is a Major Risk Factor		$2,932,558,132	70.5
4. Additional Days Required for Patients with A Secondary Diagnosis of Substance Abuse		$336,461,250	8.1
Substance Abuse Total		$4,157,444,995	

SOURCES: National Hospital Discharge Survey, 1991; 1992 HCFA Statistics; National Association of Psychiatric Hospitals Annual Survey 1992.

Chart 5

Chart 5 breaks out the substance abuse costs in terms of the four categories of costs. The largest share -- 71 percent -- of substance abuse costs are for treatment of diseases and conditions where substance abuse is a major risk factor. Direct treatment of substance abuse disorders, such as detox units, accounted for only 19 percent of substance abuse-related Medicaid costs.

Chart 6

Chart 6 details the direct treatment costs for substance abuse in general hospitals. These costs break down fairly evenly between alcohol and drugs. This chart does not include the approximately $240 million for substance abuse treatment in psychiatric facilities. The direct treatment costs in general hospitals are often not for any therapeutic treatment but, rather, for short-term treatment of immediate symptoms (e.g., stabilizing or detoxifying the patient). Costs in psychiatric hospitals include more long-term therapies such as psychotherapy and drug rehabilitation.

Charts 7-8

The next two charts portray in some detail the impact of substance abuse as a major risk factor in a variety of diseases. For 1991, 3.9 million hospital days costing Medicaid close to $3 billion dollars were due to diseases or trauma where substance abuse was a major attributable risk factor. These charts portray the pervasive impact substance abuse has on all aspects of health care. Babies born with complications due to the mother's abuse of substances during pregnancy are the major contributor to these costs and account for 32% of all Medicaid hospital days. Cardiovascular diseases (15.7%) and respiratory diseases (15.7%) are the second and third leading diseases where substance abuse is a major risk factor. The Appendix shows the specific attributable risks of the various substances to diseases identified through the review of the epidemiologic literature.

Chart 6: Medicaid Direct Treatment Days and Costs of Substance Abuse

in U.S. General Hospitals, 1991

DIRECT TREATMENT CLASSIFCIATION	DAYS	% of all Direct Treatment Days
Alcohol Dependence Syndrome	290,934	
Alcohol Psychoses	65,539	
Nondependent Alcohol Abuse	23,024	
Alcohol Poisoning	931	
SUBTOTAL - Alcohol	380,428	53%
Drug Dependence	218,066	
Drug Poisoning	53,095	
Nondependent Abuse of Drugs	51,861	
Drug Psychoses	14,692	
SUBTOTAL - Drugs	337,715	47%
DIRECT TREATMENT DAYS	718,143	100%
DIRECT TREATMENT COSTS (DIRECT TREATMENT DAYS X $750/day in 1991)	$538,607,250	

SOURCE: National Hospital Discharge Survey, 1991.

Chart 7: Medicaid Days for Diseases with Substance Abuse as a Major Risk Factor

U.S. General Hospitals, 1991

Disease/ Condition	Days	% of Total Days
Newborn/Neonate Complications	1,261,366	32.3
Cardiovascular Disease	614,463	15.7
Respiratory Disease	612,974	15.7
Burns/Trauma	355,791	9.1
Neoplasms	265,899	6.8
AIDS	211,627	5.4
Cerebrovascular Disease	189,406	4.8
Pregnancy Complications	155,483	4.0
Digestive Disease	113,343	2.9
Other	129,726	3.3
TOTAL 1991 MEDICAID DAYS	3,910,078	
TOTAL 1991 MEDICAID COSTS	$2,932,558,132	

SOURCES: National Hospital Discharge Survey, 1991;
CASA Substance Abuse Epidemiologic Database, 1993.

CHART 8: DETAILED BREAKDOWN OF MEDICAID DAYS ATTRIBUTABLE TO SUBSTANCE ABUSE AS A MAJOR RISK FACTOR

Disease	Days
AIDS	211,627
Complications in Pregnancy	155,483
Abortion	1,067
Abortion Placentae	4,878
Ectopic Pregnancy	23,970
Premature Rupture of Membrane	11,163
Spontaneous Abortion	11,452
Placenta Previa	40,981
Preterm Delivery	61,971
Neoplasms	265,899
Bladder	4,077
Brain	16,923
Breast	4,183
Cervix	8,873
Colon/Rectum	16,968
Esophagus	20,396
Kidney	5,953
Larynx	15,890
Liver	3,562
Lung	77,955
Oral Cavity	21,199
Pancreas	4,497
Stomach	12,503
Ureter	1,749
Other	51,171
Respiratory Disease	612,974
Asthma	102,447
Bronchitis	50,405
COPD	125,828
Emphysema	16,754
Influenza	7,237
Pneumonia	224,787
Other Respiratory	85,517

Disease	Days
Cardiovascular Disease	**614,463**
Cardiomyopathy	5,271
Coronary Heart Disease	324,114
Endocarditis	48,894
Hypertension	21,148
Myocardial Infarction	87,741
Peripheral Vascular Disease	127,296
Cerebrovascular Disease (Stroke)	**189,406**
Trauma	**339,478**
Burns	**16,313**
Newborns	**1,261,366**
Congenital Defects	79,616
Low Birth Weight	155,006
Birth w/Cocaine Complications	1,026,744
Digestive System	**113,343**
Crohn's Disease	7,516
Pancreatitis	84,468
Peptic Ulcer	1,102
Stomach Ulcers	9,470
Duodenal Ulcer	10,787
Other	**129,726**
Dementia	8,101
Epilepsy	14,878
Hepatitis A-C	5,756
Diabetes	3,405
Leukemia	40,243
Low Back Pain	4,026
Pelvic Inflammatory Disease	35,705
Rheumatoid Arthritis	9,832
Seizures	7,780
Total 1991 Days	**3,910,078**
Total 1991 Medicaid Costs	**2,932,558,132**

**Numbers may not add to total due to rounding*

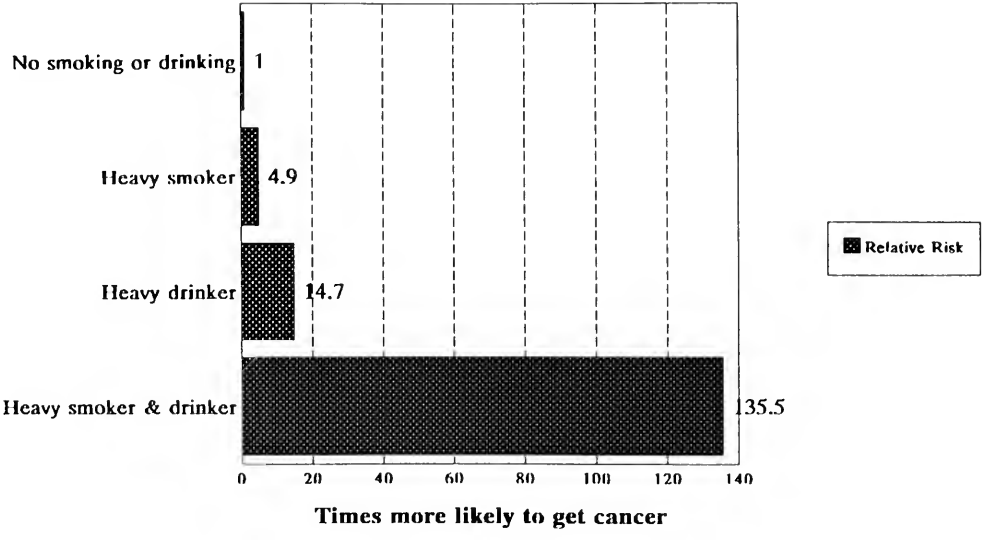
Chart 9

The attributable risks used for this study may understate the impact of substance abuse in precipitating some diseases because they were primarily based upon only one substance. People who abuse multiple substances have a much higher risk of getting these diseases than those who abuse only one substance. Our PARs do not take into account the synergistic effect of the abuse of multiple substances in part because epidemiologic research has not thoroughly assessed the synergistic effects of poly-substance use, and because prevalence rates for people who abuse more than one substance -- on Medicaid or in the general population -- are not available.

Chart 9 highlights the synergistic effect of dual-drug use: heavy drinking combined with heavy smoking dramatically increases the risk of throat cancer. People who smoke and drink are 135 times more likely to get throat cancer than those who abstain from both. In addition, they are 27 times more likely to get this disease than people who only smoke. This is also true for oral cavity cancer. Those who drink and smoke are 24 times more likely to contract oral cavity cancer than those who do not smoke or drink; they are 10 times more likely to contract this cancer than those who only drink.

Chart 9: Heavy Smoking and Drinking Increases the Risk of Throat Cancer Synergistically

Relative Risks for Hypopharyngeal/Epilaryngeal Cancer by Substance Abuse



SOURCE: Tuyns. Cancer of Larynx/Hypopharynx, Tobacco & Alcohol. Int. J. Cancer: 41, 483-491 (1988).

Charts 10 - 14

Charts 10 through 14 highlight the differences in length of stay for Medicaid patients with and without a secondary diagnosis of substance abuse -- by substance, by age and sex, and by selected diseases and conditions. As noted in the methods section, our estimates of the additional days of care required to treat patients with a secondary diagnosis of substance abuse are limited by the medical reporting of these problems.

Cigarette smoking is rarely if ever recorded as a secondary diagnosis: yet, for some conditions such as pneumonia continued heavy smoking lengthens the course of recovery.

Even for alcohol and drugs, studies show that as much as 60% of cases with secondary substance abuse problems go unrecorded. If true, many patients who have a substance abuse problem are incorrectly placed in the category of patients with no secondary diagnosis; since they have a longer average length of stay (ALOS), they artificially inflate the ALOS for the category without a substance abuse diagnosis, thus reducing the true difference in length of stay.

Moreover, the data can demonstrate a longer length of stay for many diseases where substance abuse is a comorbid condition, but they cannot portray the greater intensity of care that many of these patients must receive as a result of a substance abuse problem. As discussed above, many of the additional burn days may be spent in the Intensive Care Unit (ICU) where additional costs per day are much higher than the $750 average daily cost we used to compute cost differences in length of stay. This also understates the cost of substance abuse to Medicaid.

Chart 10 shows that the ALOS of the Medicaid patient without a secondary diagnosis of substance abuse is 4.99 days. When a patient has a secondary diagnosis of drug abuse the ALOS jumps to 8.4 days. With a secondary diagnosis of alcohol abuse, the ALOS increases to 8.94. If the patient has a secondary diagnosis of both alcohol and drug abuse, the ALOS jumps to 9.83 days, nearly double the ALOS for the patient without a secondary diagnosis of substance abuse. These figures represent average lengths of stay, but as can be seen from Charts 12-14, some diseases demonstrate much more significant differences.

The ALOS was in fact shorter for some patients with a secondary diagnosis of substance abuse. This does not imply that these patients benefitted from the use of alcohol or drugs. Rather, the differences probably result from an aberration in the data due to the small sample of patients within these diagnoses, or from the financial or social undesirability of these patients, which can lead to early discharge or transfer (dumping) to another facility. More research is needed to examine the disposition of such patients with respect to inadequate or incomplete medical care, or a lack of sufficient attention to treating their substance abuse problem.

Chart 11 compares the ALOS by sex and age for those with and without a secondary diagnosis of substance abuse. Males stay 4.2 days longer with a substance abuse problem, and females 3.1 days longer.

Much of the difference in ALOS in the under 15 age group is accounted for by the effect of substance abuse on newborns (see the next chart). Note that the ALOS is greater for both genders and all age levels for those with a secondary diagnosis of substance abuse with the exception of males in the 15-44 age bracket. Given the fact that Medicaid covers men in much

of the age range from 21 to 64 only when they have a serious and permanent disability, the "undesirable" hypothesis described previously may explain this, since this group includes those with chronic alcohol or drinking problems as well as those diagnosed as having both mental illness and chemical dependency problems. Hospitals may stabilize these individuals and then discharge or transfer them quickly to nursing homes or psychiatric facilities, accounting for their shorter length of stay.

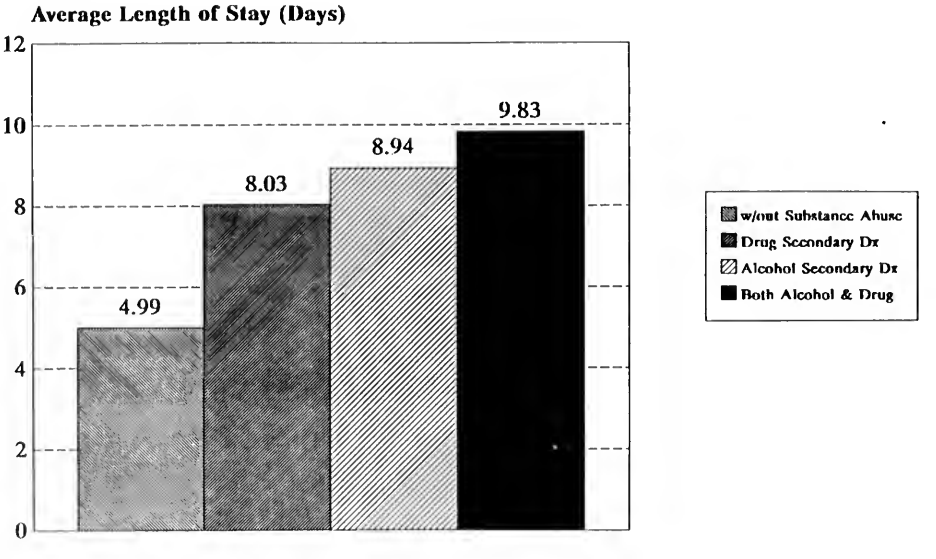
According to **Chart 12**, babies born to mothers who abuse substances during pregnancy remain almost three times longer in the hospital than babies born to mothers who did not abuse substances. In utero substance abuse exposure often results in low birth weight, premature delivery, and its sequelae, mental retardation, and congenital malformations. Here again, the difference in ALOS does not include the effect of smoking during pregnancy, which would likely make these differences even more dramatic since smoking is associated with low birth weight and other adverse effects.

Chart 13 reveals that AIDS patients with substance abuse as a secondary diagnosis stay about one-third longer than those without this diagnosis. Nationwide, 32% of all adult and 55% of all pediatric AIDS cases are attributable to intravenous drug use. Considering that AIDS is a protracted disease that may take ten years or more to run its course and involves multiple hospital stays, the total impact of even a third longer length of stay has significant cost implications.

Medicaid patients with a primary diagnosis of burns, pneumonia, or septicemia and a secondary diagnosis of substance abuse stay more than twice as long in the hospital as Medicaid patients with the same primary diagnosis but no substance abuse (**Chart 14**). For example, burn patients with a secondary diagnosis of substance abuse have an ALOS of 12.6 days compared to 5.6 days for burn patients without the secondary diagnosis.

Chart 10: Medicaid Length of Stay

With and Without Substance Abuse Secondary Dx



SOURCE: National Hospital Discharge Survey, 1991.

Chart 11: Medicaid Average Length of Stay, 1991

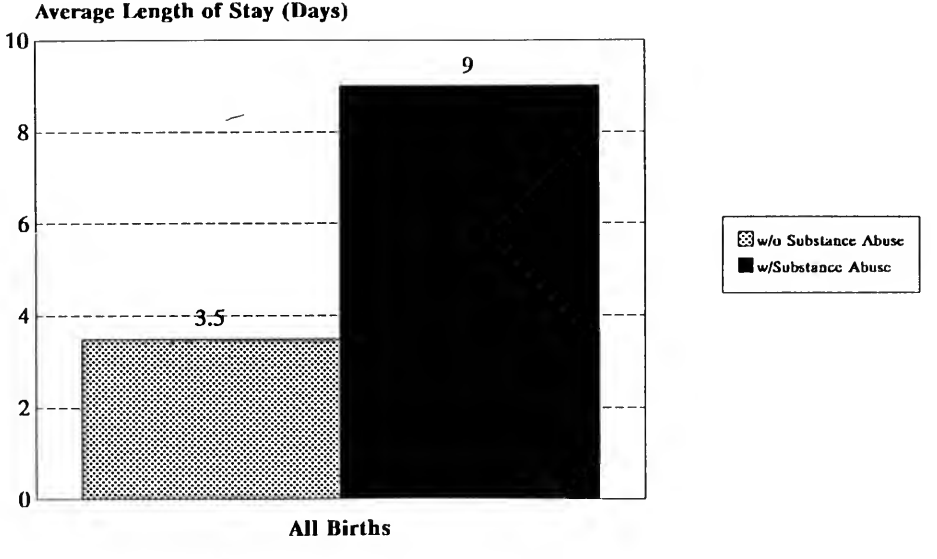
W/ and W/out Secondary Diagnosis of Substance Abuse

	Without Substance Abuse	**With** Substance Abuse	Total Additional Costs
Male	5.5	9.7	$101,577,000
<15	3.9	16.4	
15-44	9.9	8.8	
45-64	8.2	9.9	
65+	8.9	14.8	
Female	4.3	7.4	$234,884,250
<15	3.6	9.8	
15-44	3.7	6.8	
45-64	8.6	8.6	
65+	11.0	12.3	
TOTAL			$336,461,250

SOURCE: National Hospital Discharge Survey, 1991.

Chart 12: Babies Exposed to Substances Stay Longer

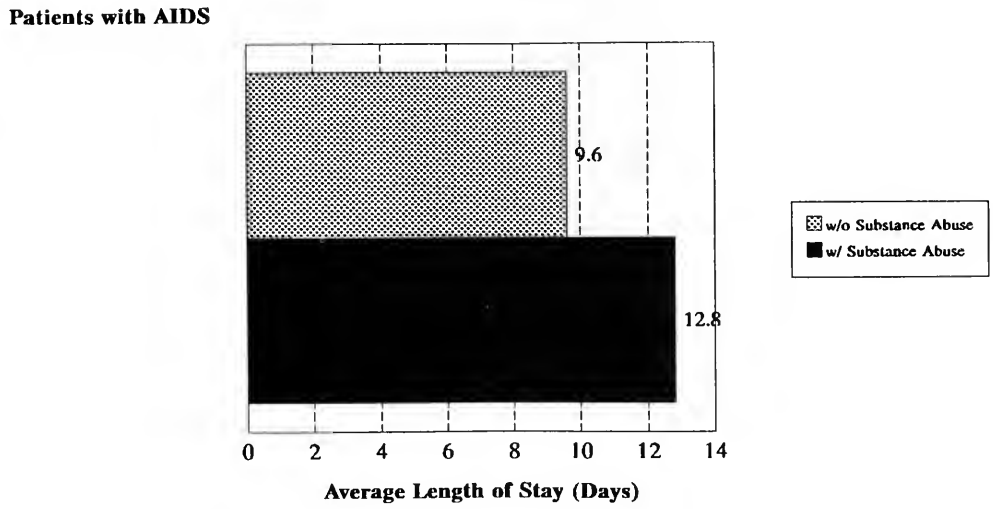
Average Length of Stay for Babies with and without Exposure to Substance Abuse



SOURCE: National Hospital Discharge Survey, 1991.

Chart 13: AIDS Patients with Secondary Diagnosis of Substance Abuse Stay Longer

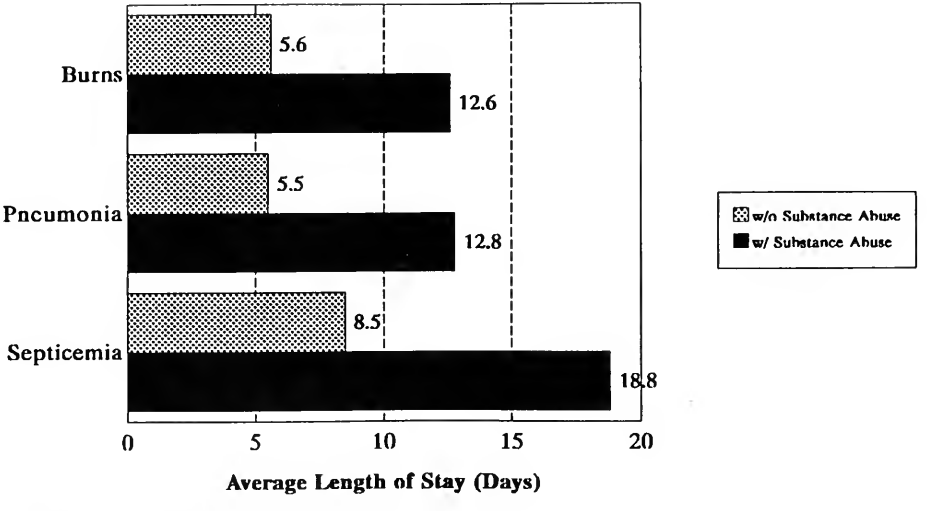
Average Length of Stay for Medicaid AIDS Patients with and without Substance Abuse



SOURCE: National Hospital Discharge Survey, 1991

Chart 14: Medicaid Patients with Secondary Diagnosis of Substance Abuse Stay Longer

Average Length of Stay for Medicaid Patients with and without Substance Abuse



SOURCE: National Hospital Discharge Survey, 1991.

Chart 15

This chart details the percentage of individuals in both the Medicaid and general populations who use each respective substance. The prevalence of drinking and drug use are projected from national figures from the National Health Interview Survey data adjusting for a larger female to male ratio in the Medicaid population (females have a lower drinking rate) and for a lower socio-economic status (those in lower socio-economic status have higher drinking prevalence). The figures do not account for overlapping use of drugs.

Medicaid-specific smoking prevalence rates by age and sex were obtained from the National Medical Expenditure Survey. The significantly higher percentages for smoking among the Medicaid population are of concern, particularly since these figures are most pronounced for women during their reproductive years.

The numbers on alcohol and drug use are self-reported. Since individuals tend to be reluctant to admit to alcohol abuse or illegal drug use, consumption rates for heavy alcohol use or drug use are likely to be significantly understated for the whole population, not just for Medicaid.

Chart 15: Consumption Rates for Medicaid and General Population

Substance	User category	Consumption Rate	
		Medicaid	General
Cigarettes	Current Smokers	42.7%	29.6%
	Former Smokers	14.3%	23.3%
Alcohol	Heavy Drinkers	10.4%	8%
Illicit Drugs	Drug Users	6.8%	5%

SOURCES: National Medical Expenditures Survey, 1987; National Health Interview Survey, 1991.

Chart 16

Chart 16 details how many pregnant women in the Medicaid population continue to smoke. These figures reflect an assumption that the 15% of Medicaid women stop smoking when they realize they are pregnant (the percentage that applies to women in lower socio-economic categories) as contrasted with a 21% decrease in smoking for women of higher socio-economic status.

The higher female to male ratio in the Medicaid population than in the general U.S. population, combined with a higher rate of cigarette smoking for Medicaid women during their reproductive years, contribute to the high Medicaid costs for birth complications and disorders.

Chart 16: Prevalence of Smoking in Pregnant Women

Medicaid and General Population, 1987

	Medicaid	General
Smoking Status:		
Current	43.7	23.4
Former	15.6	21.2
Never	40.8	55.4

Source: National Medical Expenditure Survey, 1987; Health, United States, 1991
National Health Interview Survey, 1990

Chart 17

In an era of competition, prospective payment and cost-consciousness, patients with comorbid substance abuse problems are less attractive to most hospitals. Since they are likely to use more resources, they may be less profitable to the institution than a patient without such complications. Patients perceived as socially and financially undesirable can place a hospital at a competitive disadvantage.

This problem can be seen most dramatically with respect to Medicaid where some form of prospective payment is used as the basis for reimbursement. For example, as Chart 17 indicates, patients with a secondary diagnosis of alcohol or drug use have an average case mix index that is 41% higher than for those patients without a secondary diagnosis. The case mix index is a measure of resource consumption for patients for a given group of diagnoses and often serves as the basis for payment. However, these patients stay on average 68% longer in the hospital than patients without a substance abuse problem. Thus, they may be more expensive than level of reimbursement would reflect. As a result, those hospitals that have a larger share of patients with substance abuse as a comorbid condition may be at serious financial disadvantage. This, in turn, makes such patients less attractive, and limits their access to hospital care.

Chart 17: Substance Abusers May Be Unprofitable Patients to Hospitals

	Case Mix	Length of Stay
Patients with a Secondary Dx of Substance Abuse	1.03	8.4
Patients without Substance Abuse	0.73	5.0
% Difference	41%	68%

SOURCE: National Hospital Discharge Survey, 1991.

IV. POLICY IMPLICATIONS

At least one in five dollars that Medicaid spends on hospital care is related to substance abuse. This finding of the CASA study, combined with its identification of over 70 medical conditions attributable in whole or in part to substance abuse, has profound implications for substance abuse prevention and treatment under the Medicaid program. Moreover, given the pervasiveness of smoking, and alcohol and drug abuse through all segments of American society, the implications go beyond Medicaid to the entire health care system in this country.

Investing in Research

We need to increase our support for research that will tell us what works in prevention and treatment, for whom, and at what cost. Through the Federal Agency for Health Care Policy and Research and the National Institutes of Health, we are currently investing a considerable amount of money in evaluating and identifying more cost-effective treatment approaches for a variety of medical problems. Given the tremendous cost of substance abuse and its impact on such a wide range of medical problems, greater investment in evaluating substance abuse treatment may yield even greater benefits in reducing morbidity and costs.

In addition, with respect to basic research into the causes of diseases, the Federal government invests almost $10 billion studying diseases such as AIDS, cancer and cardiovascular diseases. Yet, it spends only 5% of that amount on research into what causes substance addiction and abuse, a major risk factor for these and many other ailments.

Finally, while a considerable body of epidemiologic research already exists identifying the

relationship between various substances and morbidity, there are still many gaps in our knowledge base. The interaction of smoking with a wide range of diseases has been well established; yet, the research is much less thorough with respect to alcohol, and is even more sketchy for legal and illegal drugs. It is important that we get a better understanding of the risks presented to us by these substances separately and synergistically.

Guaranteeing Treatment

We need to ensure that appropriate substance abuse treatment and continuing care is available to all who need it and is covered in all public and private insurance programs. This includes coverage for treatment of all substance abuse, including cigarettes.[7] Currently, the Medicaid program has no explicit substance abuse treatment benefit and no mandate that the states provide such services. Limitations on the kinds of facilities and counselors who can be reimbursed further restricts access.[8]

Treatment in general appears to suffer from misplaced priorities. In a short-sighted effort to cut costs, and due to skepticism about treatment effectiveness, the Administration, Congress, and private payers have been cutting back on the kinds of treatment that they cover. The reduction in private coverage shifts more of the cost back to the public sector, including Medicaid.

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[7] *For Medicaid, the number of women in the reproductive years who smoke, combined with high rate of birth complications, argues strongly for smoking cessation programs.*

[8] *Medicaid is an underused resource with respect to substance abuse. For a more complete discussion of what is possible under the Medicaid program, CASA has recently (April, 1993) prepared a study entitled "Maximizing the Use of Medicaid Under the ACCESS Demonstration Program, An Opportunity for Change."*

A distinguished working group of 19 experts in drug abuse research and treatment convened by CASA in collaboration with The Brown University Center of Alcohol and Addiction studies, concluded in March of this year, that "the inclusion of a substance abuse treatment benefit is a vital part of true health system reform." In response to this concern, the group designed a low-cost comprehensive benefit package.[9]

Increasing Access

In addition to expanding the services covered under existing programs, we need to ensure that no one who needs help is excluded by virtue of being ineligible for coverage. Currently, low-income male IV drug users between the ages of 21 and 64 are ineligible to participate in the Medicaid program.

Finally, we need to target prevention and treatment efforts to high-cost, vulnerable individuals. Services must be made more accessible to attract at-risk but hard-to-reach individuals in inner city schools, shelters, community health centers, etc. Pregnant women are a particularly important group to reach. Substance abuse-related complications of newborns account for a staggering 32.3% of all Medicaid hospital days. Yet many treatment centers will not treat pregnant women because of concerns about legal liability. The GAO estimated that only about 11% of the pregnant women in need of drug treatment actually receive care.

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[9]*This document, available through CASA, was entitled "Recommendations on Substance Abuse Coverage and Health Care Reform." The paper was issued in March of this year.*

V. PREVIOUS RESEARCH

Alcohol and Other Drug Cost Studies

At present the most comprehensive studies on the economic costs of alcohol and other drug use are those commissioned by the Alcohol, Drug Abuse and Mental Health Administration in the 1980s. Cruze (1981) and Harwood (1984) studied the combined cost impact of alcohol and drug abuse and mental illness to society. Both studies, conducted by the Research Triangle Institute (RTI), estimated the total economic impact of alcohol and drug abuse and mental illness (ADM) disorders, including the direct costs of diagnoses and treatment of patients suffering from these illnesses, indirect costs associated with loss of earnings due to reduced or lost productivity, premature death, and other related costs.

In their estimates of treatment and costs, the RTI studies refined previous estimates by "identifying specific diseases and illnesses that are related to alcohol, drug abuse, and mental illness (ADM) and allocating costs based on the proportions of the illnesses or diseases that are attributable to ADM." However, these attributable proportions were almost solely alcohol-related: no drug-related illnesses were included. In some cases, furthermore, estimates ranged from 0.2% to 70%. Nevertheless, this work did provide a analysis of the alcohol literature and established a clear link between epidemiologic research and cost analysis.

In 1988, Rice, et al updated Harwood's cost analysis. Like Harwood, Rice attempted to estimate the total societal costs of alcohol, drug abuse, and mental illness (direct health care costs only accounted for 24% of these total costs). For estimating direct health care costs, however, Rice did not use the attributable percentages employed by Harwood. Instead, she

created a methodology for addressing issues of comorbidity. Using the National Hospital Discharge Survey (NHDS), Rice first estimated the cost of alcohol, drug, or mental illness-related as a primary diagnoses following Harwood's model. Then, recognizing that secondary diagnoses of substance abuse complicates the treatment of other diseases and thus adds to hospital costs, Rice also calculated the additional days of care reported for all primary diagnoses that had a secondary ADM diagnosis. Rice acknowledges at the outset that her estimates are low, restricted by the information reported on the medical records. In fact, many studies have documented that underreporting of secondary diagnoses is common, especially for conditions such as substance abuse that do not require direct treatment but contribute to longer stays and are considered embarrassing by the patient.

Costs of Smoking

Quantifying the costs of smoking has been a major public health issue since the 1960's. Annually, the Surgeon General issues a report on smoking and health which summarizes all current epidemiologic evidence on the relationship between smoking and disease and death. The most noteworthy of these was *Reducing Health Consequences of Smoking: 25 Years of Progress*, issued in 1989, which reported smoking attributable fractions (SAFs) for ten selected causes of death using data collected in a four year, fifty state study conducted by the National Cancer Society. These SAFs represent the proportion of deaths for a given disease that could have been avoided if cigarette smoking were eliminated.

Many economic cost studies have relied on these estimates to calculate the number of smoking-attributable deaths for specific regions and the number of years of potential life lost as a result of smoking. Some have also employed these mortality statistics to estimate hospital utilization

and costs. However, mortality SAFs, which measure smokers' risk of dying of a disease, are different than morbidity SAFs, or smokers' risk of contracting a disease. Thus, mortality SAFs cannot be used reliably for estimating morbidity or hospital costs.

Recognizing the shortcomings of using mortality SAFs in estimating health care costs, Rice (1986) developed a different methodology for identifying smokers' attributable risk of using health services using NHIS data. For people who had neoplastic, circulatory, and respiratory diseases, Rice analyzed the use of hospital days and physician visits by smokers compared to non-smokers by age and sex. From these ratios, Rice was able to calculate morbidity attributable risks which she then applied to hospital and outpatient expenditures for these diseases to estimate annual smoking-related health care costs. While not as disease-specific as the mortality-based studies, Rice's methodology set a standard for estimating annual health care costs associated with smoking.

In addition to these point-in-time estimates, others have studied the lifetime costs of smoking. For example, Manning concludes that the cumulative impact of excess medical care required by smokers at all ages far outweighs shorter life expectancy. Hodgson using survey data from the National Medical Expenditures Survey (NMES) and the National Health Interview Survey (NHIS), breaks down the differences in smokers and non-smokers expenditures by payer, revealing that over the long term, payers that cover the younger age groups (i.e. private insurers and Medicaid) bear a greater burden of smokers' costs than does, for example, Medicare. These studies have current relevance in countering the arguments that measures designed to reduce smoking (e.g., increased cigarette tax) will, in fact, increase health care costs.

Other studies have estimated the costs of specific diseases (Harwood, 1985), of specific sub-populations (Phibbs, 1991; Rivo, 1990), of distinct hospital departments (Hauswald, 1989), and of state health expenditures (Rice, 1991; Spiegel, 1990) associated with one or more substance. Most of these studies employed some version of the Rice or Harwood methodology. CASA's study also starts with Rice and Harwood's previous work, incorporating both the concept of disease-specific attributable risks to substance abuse and the marginal affects of substance abuse as a secondary diagnosis.

APPENDIX

Diseases/Conditions Attributable to Substance Abuse in Epidemiologic Research

Disease Category	*Substance*	*Attributable Risks*
Abortion	Smoking	15%
AIDS - adults	I.V. Drug Use	32%
AIDS - <13 yrs.	I.V. Drug Use	55%
Anal Cancer	Smoking	46%
Angina Pectoris	Smoking	16%
Asthma	Smoking and Passive Smoke	27%
Bladder Cancer-males	Smoking	53%
Bladder Cancer-female	Smoking	43%
Brain Tumor	Smoking	20%
Brain Tumor	Alcohol	27%
Breast Cancer	Alcohol	13%
Burns	Alcohol and Drugs	25%
Cardiomyopathy	Alcohol	40%

Cataracts - Female	Smoking	6%
Cervical Cancer	Smoking	21%
Cheek and Gum Cancer	Smokeless Tobacco	87%
Cirrhosis	Alcohol	74%
Colorectal Cancer	Alcohol	17%
Congenital Defects	Smoking	21%
Congenital Syphillis	Cocaine	9%
COPD - Male	Smoking	84%
COPD - Female	Smoking	79%
Coronary Artery Disease	Smoking	74%
Coronary Heart Disease	Smoking	52%
Crohn's Disease	Smoking	59%
Dementia	Alcohol and Drugs	11%
Diabetes - Female	Smoking	8%
Duodenal Ulcers	Alcohol	5%
Duodenal Ulcers	Smoking	52%
Ectopic Pregnancy	Smoking	74%
Endocarditis	IV Drugs	75%

Epilepsy	Alcohol	30%
Esophageal Cancer	Alcohol and Smoking	80%
Head and Neck Cancer	Alcohol and Smoking	50%
Hepatitis A	IV Drugs	6%
Hepatitis B	IV Drugs	12%
Hepatitis C	IV Drugs	36%
Hypertension	Alcohol	11%
Influenza	Smoking	45%
Kidney Cancer	Smoking	33%
Laryngeal Cancer - Female	Alcohol and Smoking	80%
Laryngeal Cancer - Male	Alcohol and Smoking	94%
Leukemia	Smoking	30%
Liver Cancer	Alcohol	29%
Low Back Pain	Smoking	10%
Low Birth Weight	Smoking	42%
Lower Respiratory Illness (Acute Bronchitis & Pneumonia)	Passive Smoke	24%
Lung Cancer - Males	Smoking	88%
Lung Cancer - Females	Smoking	74%

Myocardial Infarction - Female	Smoking	76%
Myocardial Infarction - Male	Smoking	33%
Oral Cavity Cancer	Alcohol and Smokeless Tobacco	85%
Other Respir. Diseases - Male	Smoking	37%
Other Respir. Diseases - Female	Smoking	35%
Pancreatitis, Chronic	Alcohol	72%
Pancreatitis, Acute	Alcohol	47%
Pancreatic Cancer - Male	Smoking	41%
Pancreatic Cancer - Female	Smoking	19%
Pelvic Inflammatory Disease	Smoking	33%
Peptic Ulcers - Female	Smoking	29%
Peripheral Vascular Disease (PVD)	Smoking	75%
Perinatal Death	Smoking	17%
Periodontitis	Smoking	40%
Pharyngeal Cancer	Alcohol and Smoking	80%
Pneumonia-Female	Smoking	35%
Pneumonia-Male	Smoking	36%
Pregnancy - Bleeding	Smoking	19%
Pregnancy - Premature Rupture	Smoking	32%
Pregnancy - Spontan. Abortion	Smoking and Cocaine	41%
Pregnancy - Abrupt. Placentae	Smoking	42%

Pregnancy - Placenta Previa	Smoking	43%
Preterm Delivery	Smoking	25%
Renal Cancer - Male	Smoking	39%
Renal Cancer - Female	Smoking	32%
Renal Pelvis Cancer	Smoking	60%
Rheumatoid Arthritis	Smoking	17%
Seizures	Alcohol	41%
Stomach Cancer - Male	Smoking	39%
Stomach Cancer - Female	Smoking	33%
Stomach Ulcers	Alcohol	13%
Stomach Ulcers - Male	Smoking	34%
Stroke	Smoking and Cocaine	65%
Trauma	Alcohol and Drugs	40%
Tubal Pregnancy	Smoking	36%
Ureter Cancer	Smoking	71%

THE COST OF SUBSTANCE ABUSE TO
AMERICA'S HEALTH CARE SYSTEM
Report 2: Medicare Hospital Costs
May 1994

THE IMPACT OF SUBSTANCE ABUSE ON MEDICARE INPATIENT HOSPITAL COSTS

INTRODUCTION

The Annual Report of the Trustees of the Federal Hospital Insurance Trust Fund released in April 1994 projected that the Medicare program will run out of money in seven years. This projection of future insolvency for the Fund--which pays the vast majority of hospital costs for the elderly and disabled--is due in large part to the fact that Medicare payments for hospital costs continue to grow at an alarming rate, outstripping the revenues paid into the Fund.

In responding to this crisis, invariably, the proposed solutions involve raising taxes or cutting benefits. In all these discussions, however, little time is spent in thinking about how we can keep elderly people *healthy* and avert hospitalizations. The worst example of this is our failure to move aggressively on the *pervasive impact of substance abuse, including tobacco, alcohol and drugs, on both Medicare and overall health costs*. Based on our findings, $20 billion 1994 inpatient Medicare hospital payments will be due to substance abuse and addiction. If the problems of substance abuse did not exist, we would not now be concerned about the solvency of the Hospital Trust Fund. Over the next seven years, substance abuse will cost the Trust Fund almost $170 billion. For future generations worried about the continued survival of this program, over the next 20 years, Medicare will pay out more than $1 trillion for hospital care related to substance abuse.

Past studies[1-3] have provided evidence of the impact of substance abuse on health care. Further, these studies have tended to underestimate the full magnitude of the problem because they either focus on only one substance or have not taken full advantage of the epidemiologic research that relates substance abuse to virtually every major disease category.

Despite such limitations, these studies still provide a powerful argument for the inclusion of substance abuse in the cost containment debate. In addition, they demonstrate the need to understand more fully just how critical this issue is if we are to address seriously not only the concerns over the solvency of the Medicare Trust Fund, but health care reform in general.

The CASA Study

In 1992, CASA--The Center on Addiction and Substance Abuse at Columbia University--initiated a comprehensive study documenting the full extent to which all substance abuse, including alcohol, drugs and tobacco, contributes to the costs of the health care system. Combining a critical review of the medical and epidemiologic literature linking substance abuse as a risk factor for a wide variety of medical conditions, with extensive consultation with physicians and researchers knowledgeable in this area, CASA is in the process of estimating the magnitude of this problem and its associated costs.

The first phase of this project, which examined the extent to which Medicaid hospital costs might be attributed directly or indirectly to substance abuse, was completed in July of 1993.[4] This study found that at least one in five hospital days under Medicaid, or $7.4 billion of Medicaid hospital costs in 1994, could be linked with the use or abuse of alcohol, tobacco or drugs. For diseases and health conditions as disparate as cancer, stroke, heart disease, AIDS, trauma, and birth complications, substance abuse has been documented to be a major risk factor. When these health effects are considered, substance abuse takes a major toll on the Medicaid program. And these estimates are undoubtedly still low because of both the underreporting of the problem and the fact that the available research, particularly for alcohol and drugs, is incomplete in documenting the full impact of substance abuse on morbidity.

In addition, while many had argued that the effects of these substances on disease were long-term, and the results of efforts to control abuse and addiction would not be seen for many years, the CASA study found the opposite to be the case. In fact, two-thirds of the costs of substance abuse to Medicaid were related to short-term health problems including those associated with trauma, AIDS and birth complications, where the impact on health can be seen almost immediately. Efforts to control the use of these substances can lead to immediate savings to the health care system.

The current phase of CASA's work deals with the impact of substance abuse on the use of inpatient hospital services under Medicare. As suggested in a recent study reported in the Journal of the American Medical Association[3] which examined alcohol-related hospitalizations in the elderly, the costs of alcohol abuse to Medicare can be significant. But, when *all* substances--as well as *all* the health problems related to them--are considered, the costs to Medicare are astronomically higher: more than 50 times as much as was estimated in that earlier study. Using the methodology from the previous CASA study of Medicaid (described in Appendix I), but accounting for the differential impact of these substances on the elderly, as with Medicaid, substance abuse proved to be a major contributor both to morbidity and to the costs of health care for the elderly and disabled.

RESULTS

The High Cost of Substance Abuse

In 1991[a], there were 2.2 million tobacco, alcohol, or drug-related Medicare admissions which accounted for 20% of all Medicare hospitalizations. Because these substance abuse-related cases tend to be more expensive to treat than the average hospital case, the amount actually paid out by Medicare for substance abuse-related care was even higher, accounting for 23% or nearly one-fourth of the total Medicare payments for hospital care.[b] Substance abuse-related cases cost more to treat because they required almost 26% more hospital staff and other resources than Medicare discharges that are unrelated to substance abuse. We estimated that Medicare discharges for conditions where substance abuse was a major risk factor had a Case Mix Index (CMI - a measure of resource use) of about 1.51, compared to a CMI of 1.21 for diagnoses not related to substance abuse.

As displayed in Graph 1, in dollars, Medicare spent over $13 billion of its $57 billion inpatient short-stay hospital expenditures on substance abuse-related care. These amounts exceed the 1 out of 5 dollars spent in the Medicaid program for substance-abuse related conditions.

Based upon these results, it is estimated that, for 1994, substance abuse-related Medicare hospital costs will rise to $20 billion. These costs include substance abuse-related care for both elderly and disabled Medicare recipients, with the disabled comprising 12% of these costs.

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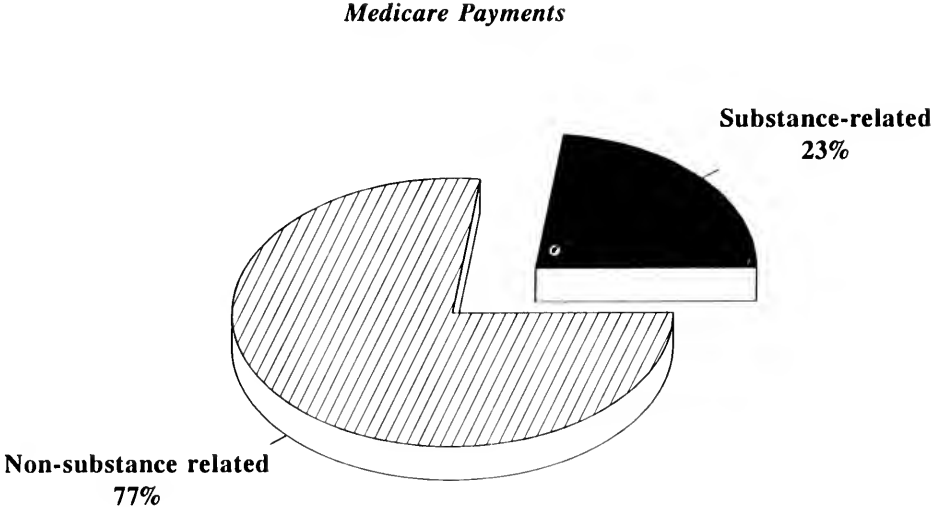
[a] 1991 is the most recent year that National Hospital Discharge Survey data is available.

[b]See Methods section for discussion of how payments were calculated.

Graph 1: Nearly 1 Out of 4 Medicare Dollars
for Hospital Care Associated with Substance Abuse



National Hospital Discharge Survey, 1991

As can be seen in Table 1, the largest share of Medicare inpatient substance abuse costs--$12.5 billion or 97% of the total--was for medical treatment of illnesses and conditions attributable to the abuse of alcohol, drugs and tobacco. These are conditions that do not mention substance abuse in the diagnosis, but are ones that have been repeatedly shown in epidemiologic research to be associated with the use of at least one of these substances.

In contrast, treatment for conditions that explicitly mention alcohol or drug abuse account for only 4% of all substance abuse-related discharges, consuming 3% of those costs. This low percentage of alcohol and drug diagnoses is misleading, and is probably more reflective of a reluctance by physicians to classify the elderly population as alcohol or drug dependent, than an indication of a low prevalence of alcohol or drug use among the elderly and disabled. Underreporting of substance abuse as either a primary or secondary condition for this population is clearly a problem as depicted in Graph 2. While 5% of all Medicare beneficiaries are considered heavy drinkers and 3% report using drugs (see Table 2), only 3% of Medicare patients in the hospital had a diagnosis that mentioned either alcohol or drug use or both. Since alcohol and drug users tend to be at greater risk for medical care, we would expect them to make up a larger, not smaller, proportion of the hospitalized population. In fact, separate studies measuring alcoholism alone among the hospitalized elderly indicate that 9-20% actually have a drinking problem.[5,6] This wide range in estimates of alcohol problems suggest that identification of alcoholism varies considerably across physicians. Thus, relying solely on diagnoses that explicitly mention alcohol or drugs on the medical record in order to measure the prevalence and cost of drugs and/or alcohol problems in hospitals grossly underestimates the full impact of substance abuse on Medicare costs.

TABLE 1: Substance Abuse Costs to Medicare

Total Hospital Care, 1991

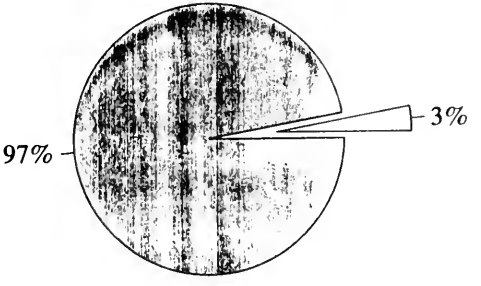
	Discharges	Expenditures
1. Direct Treatment for Alcohol and Drug Primary Diagnoses	90,659	$319 million
2. Treatment for Diseases Where Substance Abuse Is a Major Risk Factor	2,076,840	$12.487 billion
3. Additional Days Required for Patients with a Secondary Diagnosis of Substance Abuse	N/A	$112 million
Substance Abuse Total	2,167,499	$12.9 billion
Total Medicare	11.1 million	$57 billion
Substance Abuse as Percent of Total	20%	23%

SOURCES: National Hospital Discharge Survey, 1991; 1992 HCFA Statistics; National Association of Psychiatric Hospitals Annual Survey 1992.

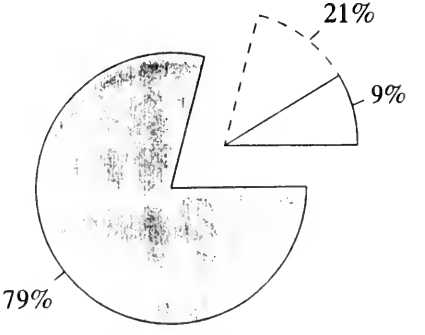
Graph 2: Underreporting of Substance Abuse on Hospital Records

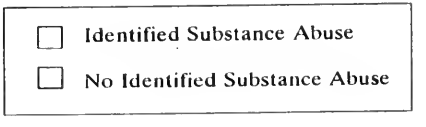
Alcohol and Drugs Recorded on Medicare Records Compared to Actual Prevalence of Alcohol Alone as Reported in Studies of Heavy Drinking in Hospitalized Elderly Populations

Alcohol and Drugs Reported on Record



Estimates of Actual Heavy Alcohol Use Alone





National Hospital Discharge Survey, 1991

Graph 2

Table 2: Consumption Rates for Medicare and General Population

Substance	User category	Consumption Rate	
		Medicare	General
Cigarettes	Current Smokers	18.4%	29.6%
	Former Smokers	36.1%	23.3%
Alcohol	Heavy Drinkers	4.8%	8%
Illicit Drugs	Drug Users	3.2%	5%

SOURCES: National Medical Expenditures Survey, 1987; National Health Interview Survey, 1991.

Drug use among the elderly also accounted for a very small percentage of the total discharges, even though more than 3% of this population admit to using drugs in the last year. This low number is, in part, indicative of a lack of research connecting illicit drugs with disease, and does not imply that drugs present no problem for the elderly. Further, since we were also unable to find sufficient data from the epidemiologic literature to quantify the health effects of the abuse of prescription drugs, we could not estimate the extent of that problem either. Thus, our estimate of the impact of drugs--both legal and illicit--on Medicare is undoubtedly low. There is clearly a need for more research to understand and quantify the impact of all drugs on morbidity and cost. Since the elderly are such large users of prescription drugs, this research is even more critical with respect to that population.

In total, we found more than 60 conditions that are associated with substance abuse covering virtually every major disease category (Appendix II)[c]. In the Medicare population, more than half of the substance abuse-related hospital admissions were for cardiovascular diseases, 15% for respiratory diseases, 12% for neoplasms, and 7% for burns and trauma (Table 3). These results differ somewhat from the earlier Medicaid study where the adverse impact on birth outcomes represented the major contributor to the costs attributable to the substance abuse. Further, in comparing substance abuse problems in the Medicaid and Medicare populations, the impact on Medicare was much more a result of the long-term effects of smoking. More than 80% of substance abuse-related Medicare hospital costs was for treating smoking-related medical conditions -- from lung cancer to chronic pulmonary

[c]This number is lower than the 72 substance-abuse related conditions identified in the Medicaid because further analysis led us to combine some specific diagnoses into broader diagnostic categories. Appendix II provides an even more detailed breakdown of the substance abuse-related discharges in all the conditions identified.

Table 3: Medicare Discharges for Diseases Attributable to Substance Abuse as a Major Risk Factor

U.S. General Hospitals, 1991

Disease/ Condition	Attributable Discharges	% of Total Attributable Discharges
Cardiovascular Diseases	1,156,057	53.3
Respiratory Diseases	328,453	15.2
Neoplasms	249,683	11.5
Trauma/Burns	149,649	6.9
Cerebrovascular Diseases	112,799	5.2
Digestive Diseases	49,798	2.3
Other	30,402	1.4
Direct Alcohol and Drug Diagnoses	90,659	4.2

TOTAL 1991 ATTRIBUTABLE MEDICARE DISCHARGES	2,167,500
1991 ASSOCIATED MEDICARE COSTS ATTRIBUTABLE TO SUBSTANCE ABUSE AS A RISK FACTOR	$12.8 billion

SOURCES: National Hospital Discharge Survey, 1991;
CASA Substance Abuse Epidemiologic Database, 1993.

obstruction disease (COPD) to coronary artery disease, as opposed to only 40% for the predominantly younger, Medicaid population.

The Medicare population is at a much higher risk for getting smoking-related diseases because people over 65 who have smoked tend to have done so more heavily and for longer time periods. Nearly 3 out of 5 of current Medicare smokers (58%) and almost one third of former smokers (32.7%) smoked an average of more than 10 cigarettes per day for over 35 years (Graph 3).

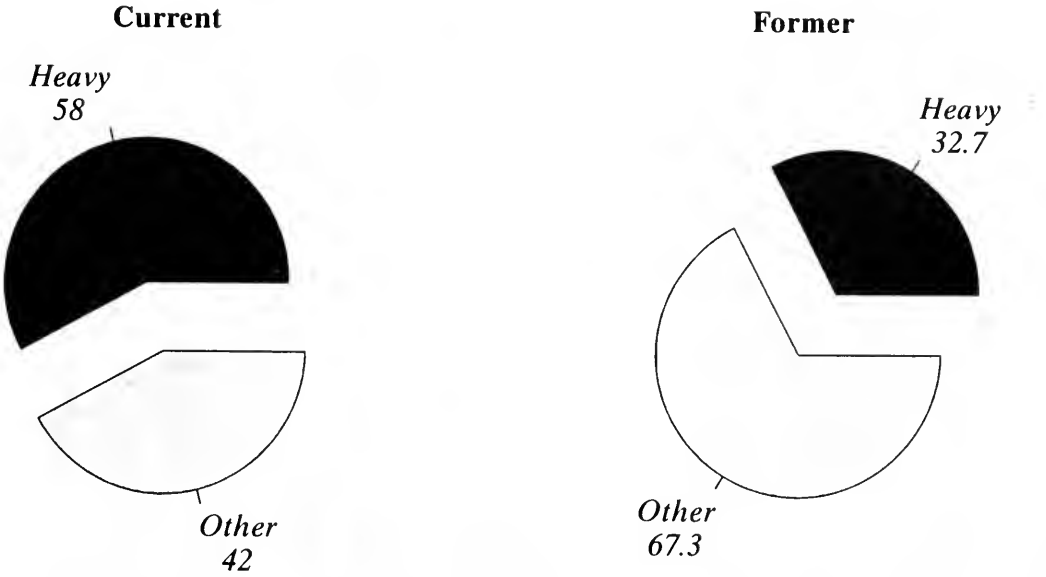
Substance Abuse as a Complicating Factor in the Treatment of other Diseases

When substance abuse is recorded as a secondary diagnosis to an otherwise unrelated condition, it tends to complicate and prolong the treatment for the underlying problem. On average, a secondary diagnosis of alcohol and/or drug abuse increased the length of time patients stay in the hospital. Compared to Medicare patients with the same primary diagnoses, those with a secondary diagnosis of substance abuse stayed an average of more than a half a day longer, 9.3 days compared with 8.6 days. While this is not insignificant, the marginal effect of substance abuse as a secondary diagnosis in the Medicare population is much smaller than what was found for Medicaid, where substance abusers stayed twice as long as non-substance abusers.

This small differential between length of stay for Medicare patients with and without substance abuse problems is most likely a significant underestimate of the full effect of alcohol and drugs as a complication. Many cases that actually involved alcohol or drug problems were not recorded as having this secondary diagnosis. Since, in our analysis, these cases would be counted in the non-substance abuse group, they may be artificially inflating the length of stay for that group. If the secondary diagnosis of substance abuse had been correctly noted, the

Graph 3: Portion of Medicare Smokers Who Have Smoked Heavily

(Those Who Have Smoked More Than 10 Cigarettes per Day for Over 35 Years)



Graph 3

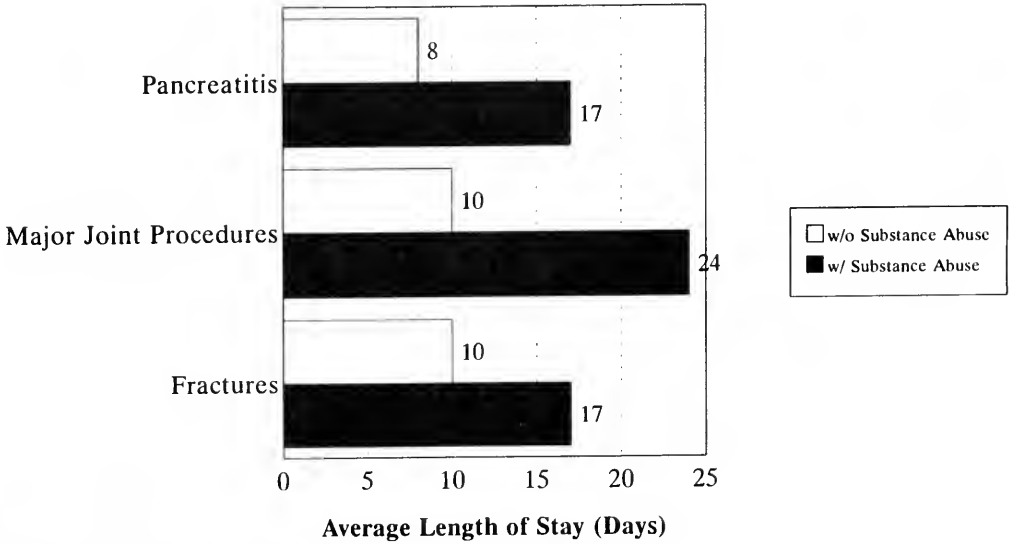
difference between the two groups would have been greater. Nevertheless, despite this problem, complications resulting from a secondary diagnosis of substance abuse accounted for $108 million in added cost to Medicare.

These figures represent average lengths of stay in Medicare but, for some diseases, the difference in length of stay was much higher. For example, for patients with pancreatitis, those requiring major joint and limb reattachments, and those with pathological fractures with a secondary diagnosis of substance abuse, patients stayed approximately twice as long as their non-substance abusing counterparts (pancreatitis 17 days vs. 8 days; major joint 24 vs. 10; pathological fractures 17 vs. 10) (Graph 4).

However, for other diseases, the ALOS was, in fact, shorter for some Medicare patients with a secondary diagnosis of substance abuse. For example, patients with respiratory infections and inflammations, cellulitis, and GI obstruction, who also had a secondary diagnosis of substance abuse, stayed less time in the hospital than non-substance abusers (e.g., respiratory infections 8.4 days vs. 11.7 days, cellulitis 7.4 vs. 8.6, and GI obstruction 3.7 vs. 7.4) This does <u>not</u> mean that patients with substance abuse needed less care. There are several possible explanations for why these substance abusers had shorter lengths of stay. It may result from an aberration in the data due to the small sample size of patients within these diagnoses, or because of the premature departure caused by some patients signing out against medical advice. However, it may also reflect the financial or social undesirability to hospitals of many of these patients which, in turn, may lead to their early discharge or transfer to another facility. In this context, it is worth noting that, if this hypothesis is true, as the forces of competition in health care intensify, these results suggest that such "undesirable" patients may be increasingly pushed out prematurely from some institutions. Further, the nature of the

Graph 4: Conditions Where Medicare Patients w/ Substance Abuse Stay Longer

Average Length of Stay for Medicare Patients with and without Substance Abuse



Graph 4

SOURCE: National Hospital Discharge Survey, 1991.

DRG payment itself-- with an implicit limit on the days of covered care--also may work against patients with substance abuse as a complicating factor to another health problem. Far more research is needed in this area.

While this study focused on substance abuse in short stay general hospitals, Medicare also pays a significant amount in psychiatric hospital costs. According to a survey of psychiatric hospitals, 15.6 percent of total admissions were for alcohol and drug abuse-related disorders. This does not include cases where another diagnosis may have been recorded or the substance abuse was secondary to a mental health problem. But, applying this percentage to Medicare psychiatric costs, in 1991 Medicare spent an additional $160 million on care for substance abuse in psychiatric hospitals.

CONCLUSION

Substance abuse is a pervasive problem that is not limited to one segment of our society. Rather, old and young and rich and poor are all equally vulnerable to its effects on their health. Further, substance abuse cannot be viewed only as a single disease entity, but must be considered as a problem that permeates every aspect of our health system and is a risk factor for all major disease categories. Not only must physicians concerned with addiction medicine address this issue, but *all* physicians, regardless of specialty, must be aware of the fact that alcohol, tobacco and drugs are a major factor in both causing and complicating the medical problems of their patients. Thus, physicians--as well as other health care professionals--must be both capable of, and willing to identify substance abuse and take the steps necessary to address it. This may range from discussions with their patients about their substance abuse problems to referral to appropriate treatment.

But, the problem does not rest solely upon the shoulders of health care providers. What has been sorely needed in the discussions of how to contain health care costs is a discussion of how we can improve our health and reduce the morbidity that leads to those costs. To do so, we need to acknowledge the importance of substance abuse as a major factor in causing and complicating the health problems of our citizens. As a nation, we have not yet made the commitment to address the problem of substance abuse. For example, the U.S. is the only industrialized nation among a group surveyed which had a tobacco tax that amounted to less than 50% of the cost of a pack of cigarettes. U.S. total taxes amounted to only an average of 30%. In addition, most other countries have considerably greater regulation on all forms of tobacco advertising than does the U.S. Among 19 countries rated in terms of their control of advertising, the U.S. ranked 18th.[7]

Nor have we invested sufficiently in the research necessary to identify and target effective interventions, or even to understand fully the relationship between various substances and illness. As we found in our own work, while there has been extensive epidemiologic research linking cigarette smoking and a variety of diseases, fewer studies relate alcohol to disease, and even less is known about the full impact of illegal drugs.

Whether, in the end, we discover that substance abuse is responsible for 20 or 30 percent (or more) of health care costs may be less the issue than the fact that we already know that literally hundreds of billions of dollars are spent each year on health care as a result of substance abuse. As a result, the future solvency of the Medicare Trust Fund is inextricably intertwined with what we do *today* to reduce substance abuse in all its forms--among our citizens. Preventing diseases that result from substance abuse and prolonging a healthy life for the elderly can be a much more potent weapon against rising Medicare expenditures than the

multitude of other, more frequently discussed cost-containment measures or benefit reductions. If there were no substance abuse, the Trust Fund's solvency would not be in doubt for almost twice the period than the Trustees are now projecting.

But this issue extends beyond the Medicare program. Debating the broader issues surrounding health care reform without either acknowledging the impact of substance abuse, or including the prevention and treatment of this problem an integral part of that reform, will be a costly mistake, making it impossible to provide universal access at all; or at a cost that, as a nation, we can afford.

APPENDIX I: METHODS

The methodology for this study relied primarily on the existing epidemiologic literature, as well as on consultations with physicians knowledgeable about substance abuse and related disorders.

Epidemiologic Literature Search

We conducted a Medline search of epidemiologic or etiologic studies that identified substance abuse (tobacco, alcohol, or drugs) as a major risk factor for acquiring a given disease/condition. In this search, we selected individual studies, reviews, or meta-analyses, that quantified either a relative risk or an attributable risk, and that generally met the criterion established by the Surgeon General for establishing causality.[8] Specifically, we favored studies that 1) reported stratified relative risks by levels of consumption or by age and sex, 2) demonstrated a dose-response relationship, 3) found diminishment of risk upon cessation of use, and 4) had findings that were generally consistent with other studies. In addition, with a very few exceptions, we used studies that measured the abusers' increased risk of **acquiring** a disease relative to a non-substance abuser (morbidity studies), as opposed to their increased risk of **dying** of the disease (mortality studies).[****]

Studies that were reviews or meta-analyses of other studies took priority since they combined the results of multiple studies and often reported a composite attributable or relative risk. If these were not available, we selected large prospective or case-control studies and calculated an average relative risk from these studies. When possible, we selected studies that

[****] A complete bibliography is available from CASA.

were targeted at the elderly population. However, we found that the elderly population is not often the focus of medical or epidemiologic research. In lieu of elderly-specific relative risks, we used relative risks for the general adult population.

Population Attributable Risk

Relative risks in epidemiologic studies are calculated by dividing the incidence of disease in the exposed group by the incidence in the disease in the non-exposed group.[9] Some researchers go one step further and calculate the risk, not just for the individual, but to the larger community, by measuring the Population Attributable Risk (PAR). The PAR is the proportion of cases for a given disease that may be attributable to an etiologic factor (e.g. cigarette smoking) and is calculated using the following formula:[9]

$$PAR = \frac{b(r-1)}{b(r-1)+1} \times 100$$

where **b** = prevalence of substance use in the population

r = relative risk for a given disease

For each disease or medical condition where a substance abuser's relative risk was reported in the epidemiologic literature, we calculated a Medicare-specific population attributable risk (PAR) using relative risks reported in the studies and the specific prevalence estimates for tobacco, alcohol, and drugs in the Medicare population. Appendix II provides a listing of those conditions, the related substances and their PARs. The PAR was computed using the above formula or, where different relative risks were reported by current and former users or by level of consumption, the PAR formula was revised to reflect this specificity.

Where diseases had joint multiple PARs for different substances (smoking and alcohol), the alcohol PAR was weighted by a factor of 0.5.

For the Medicare population, we used a prevalence of 9% for heavy drinking based on studies of drinking in the hospitalized elderly population. The prevalence of drug use was obtained from the 1991 National Household Drug Survey, and smoking from the 1987 National Medical Expenditures Survey. For most smoking-related diseases, we calculated PARs using prevalences for current and former smokers with their respective relative risks (see TABLE 4 in Results). However, for malignant neoplastic disease, some scientific evidence suggests that once smokers have reached a certain threshold of smoking (more than 10 cigarettes per day for more than 35 years), their relative risk is not diminished by cessation.[10] Smoking over a long period of time may have an irreversible oncogenic effect which is not altered by quitting.[11,12] For the Medicare population over 65 we found that 32.7% of former smokers meet the criterion of having smoked more than 10 cigarettes per day for more than 35 years. For this reason, we considered this subset of former smokers to be equivalent to current smokers in the PAR calculations for cancer.

Once PARs were computed for all diseases and conditions, ICD-9-CM codes were matched to the general diagnostic categories used in much of the epidemiologic literature. For example, the lung cancer category included ICD-9 codes 162.2-.9 (malignant neoplasms of the bronchus and lung). However, if the ICD-9 codes were not specifically identified in the original study, with the assistance of a medical coder and several physician consultants, we selected ICD codes that fell into the general disease classification and then matched the PARs for that disease category with the associated ICD-9 codes (see Appendix II).

TABLE 5--ICD-9-CM DIAGNOSES WITH MENTION OF ALCOHOL OR DRUGS

	ALCOHOL
291	Psychosis, alcoholic
303	Alcohol Dependence Syndrome
357.5	Polyneuropathy, alcoholic
425.5	Cardiomyopathy, alcoholic
535.3	Gastritis, alcoholic, w/o hemorrhage
571.0	Cirrhosis, fatty, alcoholic
571.1	Hepatitis, acute, alcoholic
571.2	Cirrhosis, liver, alcoholic
571.3	Damage, liver, alcoholic, unspecified
760.71	Fetal alcohol syndrome - Alcohol affecting fetus via placenta or breast milk
790.3	Abnormal findings, alcohol in blood level
980	Poisoning by alcohol
V11.3	Personal history of alcoholism
V61.41	Alcoholism in family
V70.4	Examination, for medicolegal reasons
V79.1	Special screening for alcoholism
E860.0	Accidental poisoning by alcoholic beverage
E860.1	Accidental poisoning by other and unspecified ethyl alcohol
E860.2	Accidental poisoning by methyl alcohol medicinal substances
E860.8	Accidental poisoning by other specified alcohols
E860.9	Accidental poisoning by unspecified alcohol
E950	Suicide and self-inflicted poisoning by solid or liquid substances

	DRUG
292	Psychosis, drug
304	Dependence, drug
305	Nondependent Abuse of Drugs
357.6	Polyneuropathy, due to drugs
648.3	Pregnancy, complicated by drug dependence
655.5	Pregnancy, management affected by suspected damage to fetus from damage
760.7	Noxious influences affecting fetus via placenta or breast milk
779.4	Reaction and intoxication, drugs, specific to newborn
779.5	Syndrome, drug withdrawal in newborn
962	Poisoning by hormones and other synthetic substitutes
965	Poisoning by Opiates and related narcotics
967	Poisoning by sedatives and hypnotics
968	Poisoning by other central nervous system depressants and anesthetics
969	Poisoning by psychotropic agents
970	Poisoning by central nervous system stimulants
971	Poisoning by drugs primarily affecting the autonomic nervous system
977	Poisoning by other and unspecified drugs
E850	Accidental poisoning by analgesics, antipyretics, and antirheumatics
E851	Accidental poisoning by barbituates
E852	Accidental poisoning by other sedatives and hypnotics
E853	Accidental poisoning by tranquilizers
E854	Accidental poisoning by other psychotropic agents
E858.0	Accidental poisoning by hormones and synthetic substitutes
E858.8	Accidental poisoning by other specified drugs - central appetite depressants
E858.9	Accidental poisoning by unspecified drug

For those ICD-9 codes which explicitly mention alcohol or drug abuse in their titles, we assigned a PAR of 100%, since all of these hospital days are attributable to substance abuse. In addition, the NIAAA has identified a list of diagnoses that are completely alcohol-related (e.g. cirrhosis). These diagnoses were also assigned a PAR of 100% (Table 5).

The costs to Medicare of substance abuse treatment in psychiatric hospitals was also included in the study. This was derived from data collected by the National Association of Psychiatric Health Systems on both the use of drug and alcohol services and the prevalence of Medicare discharges.[12]

Database

To determine the Medicare hospital costs for treating substance abuse-related illnesses, we used Medicare data reported on the 1991 National Hospital Discharge Survey (NHDS). The NHDS is a nationwide sample survey of short-stay hospitals. Each NHDS record includes the patient's primary payer, demographic information, principal diagnosis and up to four secondary diagnoses (reported by ICD-9 codes), DRG category, procedures, and length of stay.

Extracting all Medicare discharges that had a primary diagnosis that fell within a given ICD-9 code for which we had a PAR, we then applied each PAR (by age or sex, if applicable) to the discharges with corresponding diagnoses. For example, approximately 111,000 Medicare hospital discharges had lung cancer as their primary diagnosis. Of these, 87% (the PAR) or 96,600 hospitalizations were attributed to smoking.

Since Medicare pays on the basis of DRGs (not diagnoses), it was necessary to analyze the data by DRGs to estimate the costs of these substance abuse-related admissions to

Medicare. For example, Medicare discharges that had a primary diagnosis of lung cancer fell into any one of 8 DRGs (depending on the procedure required or other complications) and, therefore, were paid a different amount depending on the DRG. By placing the discharges calculated above for each ICD-9 code into their appropriate DRG, we were able to adjust for the case mix index (CMI), or the relative payment level for that discharge. In this way, we were able to obtain a case-mix adjusted total for substance abuse-attributable discharges. We then multiplied these weighted discharges by the standardized national average DRG payment for 1991 ($3,974) to determine total Medicare substance abuse costs.

While adjusting for CMI allows us to capture the higher cost per discharge for certain diagnoses, it does not measure the differential impact on length of stay when substance abuse is recorded as a secondary diagnosis. To capture the incremental costs of substance abuse as a complicating factor in treating conditions unrelated to substance abuse, we also analyzed the marginal impact of substance abuse as a secondary diagnosis on hospital length of stay. For this analysis, we defined substance abuse as only those diagnoses that explicitly mention drug or alcohol use (e.g. alcohol poisoning) or that are the immediate reaction to substance use (e.g. delirium tremens).

We calculated the difference in length of stay for patients with and without these substance abuse secondary diagnoses that had the same primary diagnoses (by gender and for the under 65 and over 65 age groups) to determine the marginal days of care that were substance-abuse related. Estimating an average cost of $604 per day for these extra days, we then added these incremental costs to our total.

APPENDIX II
MEDICARE ICD-9 CODE/PAR LIST

Disease Category	Abused Substance	ICD-9 Codes	PAR
AIDS	IV D	042.0-044.9	32% >13
	IV D		55% <13
Neoplasms			
Bladder Cancer	S	188.0-188.9, 233.7	49% M
			39% F
Breast Cancer	A	174.0-174.9, 233.0	15%
Cervical Cancer	S	180.0-180.9, 233.1	28% F
Cheek and Gum Cancer	SLT	143.0-143.9, 145.0,234.8	86%
Colorectal Cancer	A, S	153.0-153.9, 154.0-154.1 230.3-230.4	33% M
			18% F
Esophageal Cancer A,	S	150.1-150.9, 230.1	100% M
			97% F
Laryngeal Cancer	A, S	161.0-161.9, 231.0	100%
Leukemia	S	204.0-208.9	20%
Liver Cancer	A	155.0-155.2, 230.8	18%
Lung Cancer	S, PS	162.2-162.9, 231.2	93% M
			83% F
Oral/Pharyngeal Cancer	A, S, SLT	140.0-141.9, 143.0-149.9, 230.0	100% M
			82% F
Pancreatic Cancer	S	157, 230.9	37% M
			31% F
Prostate Cancer	S	185, 233.4	7% M
Renal Cancer	S	189.0, 233.9	43% M
			17% F
Renal Pelvis Cancer	S	189.1	62%
Salivary Gland Cancer	SLT	142.0-142.9	10%
Stomach Cancer	S	151.0-151.9, 230.2	35% M
			28% F
Ureter Cancer	S	189.2	71%
Vulvar Cancer	S	184.0-184.9	24%
Cancer, General	S	V073, V66.2, 198.89, 199 V58.1	54% M
			22% F

Respiratory Disease

COPD	S	491.0-492.9, 493.2, 494, 496	86% M 74% F
Influenza	S	487.0-487.1	30%
Other respiratory dis.	S	510.9, 511.0-511.9 512.0-512.8, 513.0, 518.0, 518.3, 518.81, 518.82	37% M 35% F
Pneumonia	S	480.1-480.8, 481.0, 482.1-482.9, 483, 485, 486	29% M

Cardiovascular Disease

Cardiomyopathy	A	425.1, 425.4, 425.9	37% M
Cerebrovascular Disease	S, D	431.0-435.9	70% M <65 73% F <65 33% M 65+ 16% F 65+
Coronary Artery Disease	S	410.0-410.9, 411.1-411.9, 413.0-413.09, 413.2-414.09, 414.2-414.9, 427.41, 429.2-429.29, 427.41, 429.71, 429.79	64%
Coronary Heart Disease	S	413.1, 414.1, 427.1, 427.41, 427.5-427.69, 427.71, 429.79, 428.0-428.19, 428.9, 429.3	18% M 31% F
Endocarditis	IV D	421.0, 421.9	75%
Hypertension	A	401.0-401.9, 402.0-402.9 403.0-403.9, 404.0-404.9 642.0, 642.2, 642.9	18%
Peripheral Vascular Dis.	S	415.1, 416.9, 440.0-448.9 451.0-451.9, 453.1-453.9, 454.0-454.9	75%

Pregnancy Complications

Placentae Previa	S	641.0-641.1, 762.0	26% F
Premature Rupture	S	658.11, 658.13,658.2, 761.1	32% F
Spontaneous Abortion	S, C	634	37% F
Preterm Delivery	S	644.0-644.9, 656.3-656.6	18% F

Newborns

Congenital Anomalies	S	740.0-759.9	20%

IV D = INTRAVENOUS DRUG USE; S = SMOKING; A = ALCOHOL; SLT = SMOKELESS TOBACCO; PS = PASSIVE SMOKE.

Low Birth Weight	S	764.0-765.9	36%
Congenital Syphilis	S	090.0-090.9	18%

Digestive System

Cirrhosis	A	571.5	72%
Crohn's Disease	S	555.0-555.9	32%
Duodenal Ulcers	A, S	532.00-532.90	46% M
	A		3% F
Pancreatitis, Acute A	577.0		44%
Pancreatitis, Chronic	A, S	577.1	90% M
	S		33% F
Peptic Ulcers	S	533	25% M
			14% F
Stomach Ulcers	A, S	531	29% M
	A		8% F

Endocrine and Metabolic

Diabetes	S	250.0	4% F

Other

Burns	A, S, D	940.0-949.9	23%
Cataract	S	366.1,366.3,366.45,366.9	3% M
			2% F
Dementia	A, D	290.1,290.2,290.3,290.4, 294.1, 294.9	11%
Epilepsy	A	345.1,345.3,345.9	27%
Hepatitis A	IV D	70.1	6%
Hepatitis B	IV D	70.2, 70.3	12%
Hepatitis C	IV D	70.51, 70.59, 70.9	36%
Low Back Pain	S	724.2,724.5,724.8,724.9	5%
Pelvic Inflammatory Dis.	S	614-616	38% F
Peridonitis	S	522.4, 523.4	40%
Seizures	A	780.3	22%
Trauma	A, D	800.0-909.9, 921.0-939.9 950.0-959.9	25%
Tuberculosis	A	011-013, 017, 018	25%

Diseases Entirely Related to Substance Abuse

Alcohol Related	A	291, 303, 980, 950, 357.5, 425.5, 535.3, 571.0-571.3, 655.4, 760.71, 790.3, 11.3, 61.41, 70.4, 79.1, 860.1, 860.2, 860.8, 860.9	100%
Drug Related	D	292, 304, 962. 965, 967, 968, 969, 970, 971, 977, 850-854, 357.6, 648.3, 655.5, 760.7, 779.4-779.5, 858.0, 858.8, 858.9	100%

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Mr. WAXMAN. Well, thank you, Mr. Califano. That was a very powerful statement. I don't think anybody who listened to you can just be in a state of numbness recognizing the price we are paying for 30 years of not knowing and not acting on the dangers of cigarettes.

I appreciated the statement you made when you stated that you got a letter trying to intimidate you from giving your testimony today. The tobacco industry has been engaged in a pattern of trying to intimidate people. You have been sent a letter of warning, lawsuits have been filed all over the place against media figures and networks to try to keep them from feeling free to tell the story about what is going on today in these hearings and in this investigation, and as I indicated in our opening statement, there have been unreasonable requests—in fact, legal requests to this subcommittee—which will not be permitted to keep us from doing our work.

Our responsibility now is to pick up from what we know today and try to make public policy that is appropriate to the dangers of cigarettes, and we know now that cigarette smoke is the leading cause of premature death and disease. We are paying a price because, as you indicated, these figures are absolutely astounding. Nearly $1 out of $4 Medicare spends on inpatient hospital care is attributable to substance abuse, $20 billion in fiscal 1990—1994; 80 percent of that amount is due to the long-term effects of smoking cigarettes, including lung cancer, strokes, heart disease, and respiratory ailments.

We are looking at this Congress to reform our health care system, but our health care system can't be reformed if we are not going to do something to try to prevent these kinds of cost for the future. Can we hope to hold down health care costs, human suffering, premature death, without regulating tobacco?

Mr. CALIFANO. Mr. Chairman, I think that health care reform is doomed unless substance abuse across the board is attacked front and center, and I think it is essential tobacco now be regulated.

All the health care reform is, in a sense—most of the conversation, unfortunately, tends to be on what I would call sick care reform: How do we treat people? That is really closing the door of the armory after the destructive weapons are already out there, and we have got to move aggressively in this area.

Mr. WAXMAN. One of the results of not knowing for the last 30 years about the dangers of cigarettes to the full extent that we now know is that cigarettes, to everyone's amazement when they hear it, are virtually unregulated. They are not regulated by the Food and Drug Administration; they are not regulated by the Consumer Product Safety Commission.

There is a law at the Federal level that says that States refrain from selling cigarettes to minors. Is that law being enforced, and are there steps we can take to make sure that cigarettes are not sold to minors?

Mr. CALIFANO. I think the enforcement is very spotty, Mr. Chairman. It is interesting to note that in situations in which it is enforced, relatively modest fines on small businessmen who run candy stores or newspaper stands that sell cigarettes has resulted in their changing their conduct. I think it is imperative to enforce

it, because we also have to recognize that one of the ways children get hooked is by these individuals that sell them one or two cigarettes at a time. I mean it is just like a drug dealer who will give you a little bit of cocaine or a little bit of pot. The cigarette company—the cigarette retailers will give you one or two cigarettes, then they get you hooked, and then you are into it.

Mr. WAXMAN. The law in every State in this country prohibits the sale of tobacco to minors, and yet over 60 percent of smokers today started smoking when they were younger than 16—16—and over 90 percent of the smokers today started when they were under 21. So for them to have started smoking at that age, they were evidently breaking the law when they were able to obtain those cigarettes.

But smoking is not only dangerous because—to kids who start smoking, they may get addicted, but can you tell us about the link of cigarette smoking to other hard drugs?

Mr. CALIFANO. Well, Mr. Chairman, I note in the attachment to my statement, we have done an analysis. The National Institute of Drug Abuse conducts something called the National Household Survey on Drug Abuse. It is the most—involves about 30,000 households. It is the most extensive survey of its kind about drug use in America, and we—based on our analysis of that survey, it is clear to us that children who smoke, 12- to 17-year-olds, are far more likely to use illicit drugs than those who do not smoke.

I cited in my testimony the figures of all smokers. If we go to heavy smokers who are teenagers who smoked more than one pack a day, the numbers become staggering. They are 51 times more likely to use heroin; they are 105 times more likely to use cocaine; they are 111 times more likely to use crack. And this is a serious problem, there is no question about it. For teenage America, cigarettes are a drug of entry into a world of harder drugs for many, many teenagers.

Mr. WAXMAN. Mr. Califano, my 5 minutes is up for this round of questions, but I want to thank you for what you have had to tell us.

We expect the tobacco industry to cooperate with this subcommittee because we are dealing with a very important public health danger. But I, like you, want to indicate that no one should be intimidated any longer by this tactic that might have worked 10 years ago or 20 years ago of trying to intimidate. We are going to do our job on this subcommittee, we are going to treat people fairly, but we are not going to be turned aside for any reason because what we are doing is as important as anything the Congress can do when we are dealing with the health of the American people.

Thank you very much.

Mr. CALIFANO. Mr. Chairman, thank you very much.

I must say that in 35 years, most of it in public life, I have never, ever been subjected to something like that. I have never received a letter like that enclosing an order as preposterously broad as that. It was a blatant attempt to intimidate me, and, as I said, Mr. Chairman, I am not going to be intimidated on this subject.

Mr. WAXMAN. Well, I commend you, Mr. Califano.

Mr. CALIFANO. Thank you.

Mr. WAXMAN. Mr. Bliley.

Mr. BLILEY. Mr. Chairman, thank you.

Mr. Califano, you testified today that had the Government been privy to what the tobacco companies knew back when you were in office, much would have been done differently. Well, my reading of your Surgeon General's 1979 report—and, Mr. Chairman, I ask unanimous consent that it be made a part of the record.

Mr. WAXMAN. Without objection.

Mr. BLILEY [continuing]. —Reflects that it contains many of the same findings as those being touted today as new and startling revelations allegedly concealed by the tobacco companies.

[Testimony resumes on p. 320.]

[The report follows:]

SMOKING and HEALTH

a report of the Surgeon General

- ☐ The Health Consequences of Smoking
- ☐ The Behavioral Aspects of Smoking
- ☐ Education and Prevention

THE SECRETARY'S FOREWORD

On January 11, 1964, the first Surgeon General's Report on Smoking and Health was published. It created an instant—and justified—worldwide reaction. For the report, a document of impeccable scientific authority, established a frightening link between cigarette smoking and several disabling or fatal diseases.

- The report established that cigarette smoking is causally related to lung cancer in men.
- It revealed that cigarette smoking is directly related to illness and death from heart disease and other ailments; that cigarette smoking is the leading contributory cause of death from chronic bronchitis and other lung disorders.
- The report, in short, pronounced cigarette smoking a health hazard of sufficient importance in the United States to warrant remedial action.

Today, 15 years after the original report, we publish a new Surgeon General's Report on Smoking and Health. This book is more than a compendium of new data confirming the conclusions of the original report. For this document reveals, with dramatic clarity, that cigarette smoking is even more dangerous—indeed, far more dangerous—than was supposed in 1964.

- The new report, for example, presents sobering information about a subject not extensively treated in the 1964 report: women and smoking. Among other things, the evidence suggests that mothers who smoke during pregnancy face the possibility of creating long-term, irreversible effects on their babies. And as smoking levels among women go up, disease and death rates go up also: lung cancer has increased fivefold among women since 1955. Women who smoke like men die like men who smoke.
- The report sheds new light on dramatically increased risks to smokers exposed to certain occupational hazards. Workers in the asbestos, rubber, coal, textile, uranium, and chemical industries, among others, face these risks.
- And the new report, unlike its predecessor, takes up the subject of smoking among children. The percentage of girls aged 12 to 14 who smoke, for example, has increased eightfold since 1968. Among the age group 13 to 19, there are now 6 million regular smokers. One hundred thousand children under 13 are regular smokers.

This document is significant for another reason. It demolishes the claims made by cigarette manufacturers and a few others fifteen years ago and today, that the scientific evidence was sketchy; that no link between smoking and cancer was "proven." Those claims, empty then, are utterly vacuous now. Fifteen years of additional research overwhelmingly ratify the original scientific indictment of smoking as a contributor to disease and premature death. Indeed, even the cigarette industry's own research from January 1964 through December 1973, at a cost of approximately $15 million, confirmed the lethal dangers of cigarette smoking. Today there can be no doubt that smoking is truly slow-motion suicide.

In truth, the attack upon the scientific and medical evidence about smoking is little more than an attack upon science itself: an attack upon the epidemiological, clinical, and experimental research disciplines upon which these conclusions are based. Like every attack upon science by vested interests, from Aristotle's day to Galileo's to our own, these attacks collapse of their own weight.

But why, the reader may nevertheless ask, should government involve itself in an effort to broadcast these facts and to discourage cigarette smoking?

Why, indeed? For one reason, because the consequences of smoking are not simply personal and private. Those consequences, economic and medical, affect not only the smoker, but every taxpayer.

When we consider two major national problems of health policy, we find that cigarette smoking intensifies and complicates each one.

First among these problems is the spiraling cost of health care. Health care costs nationwide now amount to $205 billion a year—of which the Federal Government pays $59 billion. Smoking accounts for an estimated $5 to $8 billion in health care expenses, not to mention the cost of lost productivity, wages, and absenteeism caused by smoking-related illness; an annual cost estimated at $12 to $18 billion.

No person, given these staggering costs, can reasonably conclude that smoking is simply a private concern, it is demonstrably a public health problem also.

A second major problem is that our health care system overemphasizes expensive medical technology and institutional care, while it largely neglects preventive medicine and health promotion.

Certainly, if the government is to shift its health strategy toward preventive rather than merely curative medicine, it cannot ignore smoking. *For smoking is the largest preventable cause of death in America.* When demographers look at death rates for diseases related to cigarette smoking, they identify 80,000 deaths each year from lung cancer, 22,000 deaths from other cancers, up to 225,000 deaths from cardiovascular disease, and more than 19,000 deaths from chronic pulmonary disease—every single one of them related to smoking. That is why smoking is Public Health Enemy Number One in America.

Having established the clear danger of smoking and the legitimacy of smoking as a public health issue, however, a final question remains: How much can government usefully do to publicize the hazards of cigarette smoking; to encourage citizens to stop smoking—or not to start?

Cigarette smoking, after all, is not like most other environmental hazards. It cannot be curbed simply through massive public and private expenditures, as in the case of water pollution abatement, on which $265 billion will be spent in the next 10 years. Cigarette smoking is not subject to the same kinds of government regulation and control that are now used, for example, to check the emission of toxic substances into the environment. These hazards can be dealt with through straightforward programs of abatement and strict regulation. When it comes to smoking, there is, of course, a role to be played by regulation and by economic and other incentives. But in a free society, research and education must be the major tools of any public-health program to deal with smoking.

So the stepped-up smoking-and-health program launched by the Department of Health, Education, and Welfare a year ago is primarily one of research, education, and persuasion. I described it last year, in testimony before the House Subcommittee on Health and the Environment, in these words:

> 'Make no mistake, our efforts are to reduce smoking. But they are efforts grounded in persuasion and information that appeal to the common sense of our citizens. They are not efforts based on coercion and scare tactics. I have the greatest empathy for the millions of Americans who want to stop smoking, but who find it very, very difficult to do so...
>
> '...If our citizens...are given all the facts from government, or other sources, and still do not wish to give up a personal habit, however hazardous, then, except for protecting the rights of non-smokers, I think government can properly do no more.'

How successful can such efforts be? Quite successful, to judge from the record:

Today, more than 30 million Americans are ex-smokers. This does not include the number of people who, after considering the risks, chose never to take up the habit; they must also number in the millions.

The number of cigarettes consumed per person in the United States has declined from 4,345 in 1963 to 3,965 in 1978. In fact, per capita cigarette consumption this past year is at its lowest level in 20 years.

These facts, without a doubt, are in large part due to efforts by public health agencies and voluntary groups to inform the public about the risks of smoking.

These efforts are not mere publicity, the record suggests that every time government and voluntary agencies have intensified their efforts to spotlight the risks of smoking, more smokers have given up the habit and more have decided not to take it up.

Moreover, we know from surveys of public opinion and attitudes that the great majority of smokers (90 percent) have either tried to quit smoking or would probably quit, if only they could find an effective way to do so.

These people need help.

So, too, do millions of children and young people who must have the facts if they are to make a truly informed choice whether to smoke. Indeed, it is children who are the main focus of our efforts to inform and persuade. It is nothing short of a national tragedy that so much death and disease are wrought by a powerful habit often taken up by unsuspecting children, lured by seductive multimillion dollar cigarette-advertising campaigns.

This new Report of the Surgeon General typifies the Department's approach to the issue of smoking and health. It is based on scientific research. Its purpose is to provide facts. Its persuasive power is in the weight of the scientific evidence.

We set out to publish it for three reasons. First, we wished to bring together new information on smoking and health which has accumulated in the 15 years since Surgeon General Luther Terry released the epochal report of 1964.

Second, we wished to extend the area of inquiry into smoking and health beyond medicine into the fields of education and behavioral science. For many of the remaining unanswered questions about smoking and health are in these latter fields. We have some evidence, for example, that women smokers have more trouble giving up smoking than men—but why? Some observers believe that women are more concerned than men about gaining weight when they stop smoking. But in fact we do not know, the answers to that and other questions about smoking must be pursued through future behavioral research.

Third and finally, we wished to provide a firm base of knowledge on which health agencies throughout this nation—and the world—can build their efforts to reduce cigarette-related death and disability. For the problem of cigarette smoking is not just domestic, it is worldwide. Smokers in the United States consume 615 billion cigarettes a year; worldwide, the consumption of cigarettes approaches three trillion each year.

This, then, is the report—a compendium of 22 scientific papers on smoking and health, commissioned by the Surgeon General of the Public Health Service, compiled by 12 agencies of the Department of Health, Education, and Welfare, and reviewed by scientists who are recognized experts in their fields of inquiry. Thirteen of the papers comprise a report on the health consequences of smoking, which the Secretary of Health, Education, and Welfare is required by law to submit to Congress each year. The remaining chapters deal with behavioral aspects of smoking and with education and prevention.

This report is, in my judgment, a major contribution to knowledge about smoking and health—and a major resource for physicians, public health officials, educators, and others who are concerned with advancing the nation's health through a sound strategy of prevention.

Joseph A. Califano, Jr.
Secretary
Department of Health,
Education, and Welfare

January 11, 1979

PREFACE

On January 11, 1964, the Surgeon General's Advisory Committee on Smoking and Health concluded: "Cigarette smoking is a health hazard of sufficient importance in the United States to warrant appropriate remedial action."

Today, this report reinforces that major conclusion. It is backed up by the weight of thousands of additional studies performed throughout the world. Fifteen years later, the scientific evidence on the health hazards of cigarette smoking is overwhelming.

The information in the health consequences and behavioral parts of this report has been brought together by 10 agencies of the United States Public Health Service. As will be seen, these agencies have different research or regulatory missions but a common concern with cigarette smoking as a contributor to illness, disability, and death.

Since 1964, an estimated 30 million men and women have quit the cigarette smoking habit. The prevalence of regular cigarette smoking in the adult population has declined from approximately 42 percent to 33 percent (Appendix). Yet, in 1978, an estimated 54 million men and women smoked 615 billion cigarettes. Each year, the health damage resulting from cigarette smoking costs this nation an estimated 27 billion dollars in medical care, absenteeism, decreased work productivity, and accidents. A great fraction of these costs are borne by the entire public – smokers and nonsmokers – through health insurance, disability payments, and other private and taxpayer-supported programs. In 1979, cigarette smoking is the single most important preventable environmental factor contributing to illness, disability, and death in the United States (Chapters 2 and 3).

This 1979 report describes our current knowledge of the health consequences of smoking, the behavioral aspects of smoking, and efforts in education and prevention. It presents strong conclusions where they are warranted by the accumulated evidence. It provides alternative working hypotheses when the available facts are not sufficient to warrant conclusions. It suggests future lines of inquiry where there are gaps in existing knowledge.

Adhering to this spirit of inquiry and recognizing the magnitude of the public health problem, we must ask: What is our current knowledge about "appropriate remedial action?" What scientific, economic, and behavioral facts are important for the design of public policy toward cigarette smoking? What have we learned so far, and where do we go from here? To answer these questions, we must confront three central facts: Individuals vary in their health risks associated with cigarette smoking. Individuals vary in their cigarette-smoking behavior. The cigarette product itself is changing.

High Risk Populations

The adverse health effects of smoking vary considerably in their nature and severity among individuals. They depend, for example, on the duration and frequency of smoking, on the presence or absence of concurrent illness or other environmental exposures, and on the individual's age and sex. Some health effects are immediate, while others may be delayed for years.

Most importantly, certain individuals may be particularly prone to these adverse health effects.

Women, youth, minorities, and workers exposed to occupational hazards in no way constitute an exhaustive list of especially high risk individuals. Every chapter in this report attempts to focus on particular types of individuals of highest susceptibility. Cigarette smoking acts synergistically with hypertension and elevated cholesterol to enhance the risk of developing coronary heart disease (Chapter 4). Cigarette smoking may be a promoter or co-carcinogen among those individuals exposed to other cancer-causing agents (Chapter 5). It has been suggested that there may be groups of smokers highly susceptible to lung damage from cigarette smoke whose characteristics might be detected by pulmonary function tests and histological studies or by the presence of alpha-1-antitrypsin deficiency (Chapter 6). Those other risk factors which may make maternal smoking more dangerous to the fetus need to be isolated, such as anemia, poor cardiac function, unfavorable age, and other socioeconomic factors (Chapter 8). Individuals with rhinitis or asthma may in fact be more sensitive to the nonspecific noxious effects of smoke (Chapter 10). Cigarette smoking increases the risk of peripheral vascular disease in diabetics (Chapter 4).

Women and Smoking

The findings in the report have grave public health implications for women of all ages. Although the prevalence of cigarette smoking among adult males has declined from approximately 53 percent in 1964 to 38 percent in 1978 (Appendix), the overall percentage of adult female smokers remains virtually unchanged at about 30 percent (Appendix). Cigarette smoking among younger women has increased, particularly among teenage girls. The mortality rate from lung cancer for women in 1978 was almost three times as high as in 1964, and the ratio of male to female mortality from lung cancer has decreased by almost one-half (Chapter 5). Women who have smoking characteristics similar to men experience overall mortality rates similar to men (Chapter 2).

Cigarette smoking is a major independent risk factor for fatal and nonfatal heart attacks and sudden death in both men and women (Chapter 4). The risk of heart attack is increased about tenfold in those women smokers who use estrogen-containing oral contraceptives (Chapters 4 and 12).

The weight of evidence demonstrates that smoking during pregnancy has a significant adverse effect upon the well-being of the fetus and the health of the newborn baby (Chapter 8).

There is abundant evidence that maternal smoking directly retards the rate of fetal growth (Chapter 8) and increases the risk of spontaneous abortion, of fetal death, and of neonatal death in otherwise normal infants. More important, there is growing evidence that children of smoking mothers may have measurable deficiencies in physical growth, intellectual development, and emotional development that are independent of other known risk factors (Chapter 8). Children of mothers who smoke during pregnancy do not catch up with children of nonsmoking mothers in various stages of development (Chapter 8).

Children and Teenagers

Smoking among teenage boys has remained virtually constant, and among teenage girls it is actually increasing (Chapters 17, 18, and Appendix). The average age of experimentation with cigarettes and initiation of regular cigarette smoking has been decreasing (Chapter 17 and Appendix). Survey data suggest that teenage and early-youth smoking habits are major determinants of lifelong cigarette consumption. The mortality rates from all causes are significantly higher among those who initiate smoking earlier in life (Chapter 2).

Evidence is accumulating that the health effects of smoking evolve over a lifetime (Chapters 2, 3, 4, 5 and 6). Even when a morbid or fatal consequence of smoking occurs in later life, its antecedents may be present even in childhood. For example, autopsy studies show that cigarette smoking is associated with more severe and extensive atherosclerosis of the aorta and coronary arteries (Chapter 4). Several scientific questions have been raised about effects of smoking on the severity of atherosclerosis in childhood and adolescence and the premature development of adult forms of these lesions (Chapter 4).

Clinical, experimental, pathological, and epidemiological studies in humans and animals demonstrate that cigarette smoking produces measurable lung damage, even in very young age groups (Chapter 6). Young cigarette smokers, even those without respiratory symptoms, have evidence of small airway dysfunction more frequently than nonsmokers (Chapter 6). A number of recent studies have established a higher prevalence of regular cough, phlegm production, wheezing, and other respiratory symptoms in teenage and young adult smokers as compared to nonsmokers (Chapter 6). The connection between pediatric respiratory illness and adult chronic respiratory disease has been supported in prospective studies (Chapter 6).

Children and teenagers are susceptible in many ways to the effects of others' smoking. Numerous research studies have found a signifi-

cant relation between childrens' respiratory illness and parental smoking (Chapter 11). Childrens' cigarette smoking habits are strongly influenced by the smoking habits of family members and peers (Chapters 17 and 18).

Minorities

The health consequences of cigarette smoking in minorities may be particularly severe, yet little is known about these health consequences at present. Survey data indicate that the prevalence of cigarette smoking among blacks exceeds that of whites (Appendix). Lung cancer death rates among blacks exceed those of whites (Chapter 5). The effects of maternal smoking on fetal development and infant health may be especially significant among minority mothers with other risk factors for complication of pregnancy (Chapter 8). Nonwhite workers in industrial settings may be particularly susceptible to the combined effects of cigarette smoking and occupational exposure to toxic agents (Chapters 5 and 7).

Smoking and Occupational Exposure

In every race, sex, and age group, blue-collar workers are especially susceptible to the combined effects of cigarette smoking and exposure to toxic industrial agents (Chapter 7). Fumes from fluorocarbon polymers are decomposed by the heat of burning cigarettes (Chapter 7). These and other chemicals contaminate cigarettes, which are then smoked (Chapter 7). Cigarette smoke contains many of the same chemicals found to be workplace toxins, such as hydrogen cyanide and carbon monoxide (Chapter 7). Exposure to coal dust, cotton dust, chlorine, and radiation combine additively with cigarette smoke to produce lung damage (Chapters 6 and 7). Cigarette smoking acts synergistically with exposure to asbestos to produce lung cancer (Chapters 5 and 7). Other documented examples of synergistic action include rubber fumes, dust, and radiation from uranium mining (Chapter 7). Studies have shown that cigarette smoking contributes to accidents in the workplace (Chapter 7).

Cigarette Smoking Behavior

The design of policy depends not only on our ability to identify high-risk groups but also on our understanding of differences in the cigarette-smoking behavior of these individuals. As numerous references in Chapters 15–21 and the Appendix emphasize, there are serious gaps in our understanding of the initiation of the smoking habit, the nature of cigarette dependence and withdrawal, and the cessation of smoking. Yet to design and implement effective policies, we must know how various target groups differ in each of these dimensions.

Evidence is cited in this report that women may differ from men in the initiation, maintenance, and cessation of smoking. It has been suggested that the abstinence syndrome is more severe in women (Chapter 15). Women are apparently more likely to fail in organized cessation programs (Chapter 19). Survey data suggest an increase in the prevalence of heavier smoking among younger females entering the smoking population (Appendix).

In this respect, we need to study the effects of introducing filter cigarettes in the 1950's and 1960's and the effects of the newer lower "tar" cigarettes in the 1970's upon the initiation of smoking, especially among young women (Appendix). We need to know whether advice is effective in influencing cigarette smoking, particularly among pregnant women during prenatal care.

Among children and teenagers, the experimental phase of cigarette smoking (Chapter 17) may in fact be the critical point of intervention. It is possible, and some investigators have suggested (Chapter 17), that younger and older adolescents respond differently to different types of antismoking intervention (Chapter 17). It also remains unclear whether teenagers respond more to contemporary peer pressure to smoke or to adult smoking images (Chapter 17). If adult family members in fact have the most critical influence on teenage smoking initiation, then the critical target population may be the adults and not their children (Chapter 17). Although the literature on the responsiveness of cigarette consumption to price is conflicting, some studies suggest that the demand for cigarettes among teenagers may be more price sensitive (Chapter 18).

Survey data suggest that individuals who attempt to quit cigarette smoking have had considerably more success in rapid and complete cessation than in gradual reduction in the amount smoked (Chapter 15). Some studies in fact suggest that withdrawal symptoms are more severe during gradual reduction (Chapter 15). Other studies suggest that very few smokers can satisfy their addiction on less than 10 to 12 cigarettes daily (Chapter 16). On the other hand, there is some evidence that lighter smokers are more successful at cessation (Chapter 18 and Appendix). There is also inconclusive evidence that lower "tar" and nicotine cigarettes can be a vehicle for cessation. These results need to be reviewed in light of the emergence of new personalized programs of smoking cessation which have reported recent success (Chapter 16).

Finally, the available survey data indicate that the prevalence of smoking is higher among minorities and blue-collar workers (Appendix). Yet very little is known about motivations for initiation and cessation of smoking among these individuals.

The Changing Cigarette Product

The cigarette product itself has changed considerably in the past 25 years. In 1954, when reports linking cigarettes to lung cancer first appeared, less than 1 percent of cigarettes produced were filter-tipped (Appendix). The average "tar" delivery of cigarettes was approximately 36 mg. The average nicotine delivery was over 2 mg (Chapter 14 and Appendix). In the years following this antismoking publicity, the consumption of filter cigarettes rose rapidly, and the average "tar" and nicotine deliveries of cigarettes decreased. By 1964, at the time of the Surgeon General's first report, the market share of filter cigarettes had reached 60 percent (Appendix). The average "tar" delivery of a cigarette was about 21 mg. The average nicotine delivery was approximately 1.3 mg (Chapter 14 and Appendix).

Since then, the average "tar" and nicotine deliveries have continued to decline. This was encouraged by a series of Government actions beginning in 1966. In that year, the Public Health Service issued its finding that "the preponderance of scientific evidence strongly suggests that the lower the 'tar' and nicotine content of a cigarette, the less harmful [will] be the effect." This was followed by the decision of the Federal Trade Commission to begin measuring the "tar" and nicotine yields of cigarettes and to permit manufacturers to begin using this information in their advertising.

By 1977, the sales-weighted average "tar" per cigarette approached 17 mg, the sales-weighted average nicotine per cigarette approached 1.1 mg (Chapter 14 and Appendix). This decline in "tar" and nicotine resulted from important changes in cigarette production technology — the development of tobacco sheet reconstitution, improvements in cigarette filtration and cigarette paper, the genetic manipulation of tobacco strains, and increased use of plant stems and other tobacco portions formerly regarded as waste. In the past 5 years, the market share of cigarettes with "tar" delivery of 15 mg or less has increased dramatically and is now expected to exceed 30 percent. In 1977, nearly one-half of the cigarette industry's $0.8 billion advertising and promotional budget was devoted to these cigarettes.

How should we interpret these changes? What do these "tar" and nicotine measurements represent?

In one year, a typical one-pack-per-day smoker takes in 50,000 to 70,000 puffs through the burning column of a unique chemical factory which contains over 2,000 known compounds (Chapter 14). Many of these compounds are established carcinogens (Chapter 14) and appear in the particulate phase or "tar" of the smoke. A nonspecific decrease in "tar," however, does not necessarily imply a specific decrease in any single dangerous substance. Moreover, there is as yet no unequivocal evidence for the existence of "safe" levels of these carcinogenic chemicals. Even if we could identify and selectively eliminate certain known carcinogenic chemicals from cigarette smoke, there may be

numerous, as yet unidentified, dangerous substances remaining (Chapter 14).

In addition to "tar" and nicotine, cigarette smoke contains a gaseous phase with numerous components such as hydrogen cyanide, volatile aromatic hydrocarbons, and carbon monoxide. Carbon monoxide, in particular, has been identified throughout this report as a possible critical factor in coronary heart disease, atherosclerosis and sudden death, occupationally related illness, chronic respiratory disease, fetal growth retardation, and the noxious effects of passive smoking (Chapters 4, 6, 7, 8, and 11). At present, we do not have standard, reproducible measurements of the delivery of carbon monoxide in all U.S. cigarettes. Yet, some published studies suggest that some allegedly less harmful cigarettes may have higher concentrations of carbon monoxide. In Great Britain, the carbon monoxide delivery of certain filter cigarettes exceeded that of other nonfilter cigarettes (Chapter 14).

There is substantial experimental evidence, and some supporting data from retrospective studies, that cigarettes with reduced "tar" and nicotine delivery should in principle have reduced risks of health hazard (Chapters 2, 4 and 5). However, there is only one single controlled prospective study, quoted numerous times throughout this report, of the effect of "tar" and nicotine content on mortality rates. Such a study has not been repeated. The risks of overall mortality and specific mortality from lung cancer and coronary heart disease were lower in those smoking lower "tar" and nicotine cigarettes than in those smoking higher "tar" and nicotine cigarettes. But the risks for low "tar" and nicotine cigarette smokers were still significantly higher than in nonsmokers. This study did not evaluate the risk of mortality from other causes, such as chronic obstructive lung disease. It does not establish that low "tar" and nicotine cigarettes diminish the effect of smoking on the unborn fetus or the developing child. Moreover, the period of observation in this study was 1960 to 1972. Cigarettes regarded as low in "tar" and nicotine during this time do not represent current products. This study does not establish that currently available low "tar" and nicotine cigarettes are necessarily less hazardous.

The "tar" and nicotine content of cigarettes is measured by machines which smoke cigarettes according to a predetermined puff rate, butt length, duration of puff, and volume of puff. An individual smoker does not necessarily consume cigarettes in this standardized manner. It is possible for a low "tar" and nicotine smoker to inhale in one day much more of these constituents than a smoker of cigarettes with higher "tar" and nicotine content. Some studies suggest that individuals who smoke low "tar" and nicotine cigarettes may inhale more deeply or smoke the cigarette further down to the butt to compensate for the lower concentration of nicotine (Appendix). In other experiments, individuals given low "tar" and nicotine cigarettes

increase the number of cigarettes they smoke. In this respect, there is little epidemiological information concerning the trade-off between smoking a few higher "tar" cigarettes and smoking many lower "tar" cigarettes. A few long-term follow-up studies suggest that many smokers who voluntarily switch to low "tar" cigarettes may not increase their frequency of cigarette consumption. The interpretation of these studies is complicated, however, by our lack of understanding of the motives and circumstances of an individual's decision to switch to a lower "tar" cigarette.

The effect of a decrease in "tar" and nicotine content applies not only to changes in the habits of current smokers, but also to the cigarette consumption of potential new smokers (Appendix). Although there is no conclusive evidence on this point, we need to know whether the lowering of "tar" and nicotine in cigarettes over the past 20 years has made it easier for our youth to experiment with and later become habituated to cigarettes (Appendix).

Finally, the successful marketing of these low "tar" and nicotine cigarettes has required the addition of numerous flavor additives. The nature and composition of these additives is to some extent a proprietary matter. Nevertheless, we do not know whether these undisclosed additives are themselves harmless.

Until these scientific and behavioral issues are resolved, there can be no final assessment of the public health benefits of our present search for less hazardous cigarettes. The preponderance of scientific evidence continues, as in 1966, to suggest that cigarettes with lower "tar" and nicotine are less hazardous. It has become clear in the years since, however, that in presenting this information to the public three caveats are in order: Consumers should be advised to consider not only levels of "tar" and nicotine but also (when the information becomes available) levels of other tobacco smoke constituents, including carbon monoxide. They should be warned that, in shifting to a less hazardous cigarette, they may in fact increase their hazard if they begin smoking more cigarettes or inhaling more deeply. And most of all, they should be cautioned that even the lowest yield of cigarettes presents health hazards very much higher than would be encountered if they smoked no cigarettes at all, and that the single most effective way to reduce the hazards associated with smoking is to quit.

Public Policy

The decision to smoke is a personal decision, but once this is said, it remains unquestionably the responsibility of health officials to insure that smokers and potential smokers are adequately informed of the hazards. This is especially true in a society where hundreds of millions of dollars are spent each year promoting cigarettes and where these and many other influences are encouraging young people to take up smoking.

The consideration of what is meant by "adequately informed" is a scientific and public health policy problem.

As this report shows, our knowledge of the relevant facts regarding the health hazards of cigarette smoking has increased manyfold since 1964. And efforts at adequately informing the public have had some success. According to survey data (Chapter 16), a majority of smokers, both adults and teenagers, respond affirmatively to questions about the health hazards of smoking and the desirability of quitting. Yet, perhaps because nicotine is a powerful addictive drug, millions of smokers seem unable to translate this information into personal action. Further, we know so little about how to prevent smoking among children and teenagers that the numbers of new smokers have remained virtually constant.

Earlier in this preface we noted changes that have taken place in the composition of the smoking population, in smoking behavior, in the character of the cigarette itself, and in smoking risks. We must take these changes into account in our efforts to inform. If we can now identify groups of people who are at high risk, what interventions can we design to reach them? Have previous educational efforts been too broadly based? Do the changes in the nature of the cigarette argue for a shift in emphasis, from less hazardous cigarettes to less hazardous smoking? Are there specific instances where the weight of the scientific evidence and the magnitude of the health problem require action by society, other than merely imparting information?

In addressing these questions, we must be sure we are active rather than reactive in our approach. The hazards of cigarette smoking have been established and the question has turned to what society's response to these hazards should be. If this report is successful, it will encourage the medical and public health communities to continue their search for what the Advisory Committee 15 years ago defined as "appropriate remedial action."

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Assistant Secretary for Health
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January 11, 1979

Behavioral Aspects of Smoking

Because of the research over the past 15 years, much is now known about the health dangers of smoking. But research into reasons why the habit is so widespread and difficult to break is still in its infancy, little is known for certain, and questions far outnumber answers.

This part of the report summarizes current understanding of the biological, behavioral, and psychosocial aspects of the cigarette smoking habit and the dependence process associated with smoking. It is no exaggeration to say that smoking is the prototypical substance-abuse dependency and that improved knowledge of this process holds great promise for prevention of risk. Establishment and maintenance of the smoking habit are, obviously, prerequisite to the risk, and cessation of smoking can eliminate or greatly reduce the health threat.

Among the findings, tentative conclusions, and areas for research presented in this section are the following:

1. Nicotine, the most powerful pharmacological agent in cigarette smoke, has been proposed as the primary incentive in smoking and may be instrumental in the establishment of the smoking habit. The proposition that heavy smokers adjust their plasma nicotine levels is compatible with the observation that regular smokers commonly consume about 20 to 30 cigarettes during the smoking day (approximately one every 30 to 40 minutes) and that the biological half-life of nicotine in humans is approximately 20 to 30 minutes.

2. Recent research suggests that specific central nervous system receptor sites for nicotine can be blocked in a fashion analagous to the opiate antagonists. This phenomenon has implications for understanding the effect of nicotine on the body as well as in helping former smokers to maintain abstinence.

3. By far the most common, and clinically the most important, symptom to appear following withdrawal from tobacco is craving for tobacco. The importance of the tobacco-withdrawal syndrome is its provocative role in relapse among abstinent smokers. Abrupt and total withdrawal from tobacco is associated with a withdrawal syndrome that subsides more quickly and is no worse than that seen in partial abstinence. A partially-abstinent smoker is in a chronic state of withdrawal that typically leads to relapse and a return to baseline rates of smoking.

4. There is fragmentary evidence suggesting that the abstinence syndrome is more severe in women than in men, and it seems likely that this is at least partly responsible for lower rates of successful cessation among women.

5. Little is known about the millions of smokers who have quit on their own. It has been estimated that 95 percent of the 29 million smokers who have quit since 1964 have done so on their own.

6. Survey data show that only one-third or less of smokers motivated to quit are interested in formal programs, and only a small minority of those who do express an interest actually attend programs when offered. It thus appears that available objective outcome data may be based on a small minority sample of smokers at large.

7. Objective data are lacking on most of the smokers who have been willing to attend formal programs. Public service clinics continue, but lack of objective outcome data precludes the evaluation of their efficacy. Similarly, proprietary programs remain virtually unmonitored and unevaluated in an objective fashion. Controlled research has yet to produce a clearly superior intervention strategy. However, rapidly accumulating and improving data now suggest that multi-component interventions offered by intervention teams with practical knowledge regarding the smoking problem are the most encouraging.

8. Too few carefully designed and implemented longitudinal studies exist in the area of smoking in children and adolescents to allow for true evaluation of the effectiveness of many past programs developed for them.

9. Inferences about the evolution of smoking suggest that by the end of the ninth grade very few adolescents are addictive smokers; the critical level of the onset of addictive smoking appears to be in high school. Therefore, the true impact of any deterrence-of-smoking program with adolescents may not even be measurable until after the adolescent has entered high school. This problem is not unlike the recidivism encountered in virtually all smoking cessation programs.

10. Too many programs for youth have focused on information about smoking or fear of serious disease due to smoking. Adolescents are present-oriented and appear to be less influenced by messages concerning smoking that focus exclusively on long-term dangers.

11. A focus on research into prevention of the onset of addictive smoking appears to be a reasonable parallel course to follow along with efforts at control and cessation.

12. A promising new approach may be in the "inoculation" of adolescents against various pressures to smoke which apparently override their knowledge about the dangers of smoking. The approach involves strategies to resist peer pressure, emphasis on understanding of how advertising and mass media work to influence smoking, and provision of information on ways to resist the models of parents, siblings, and older students who smoke. Also included is a focus on the immediate physiological effects of smoking rather than on long-term effects.

Education and Prevention

Research strongly indicates that educators and health care providers teach youth about smoking and health as much by example as through formal instruction. But, despite a proliferation of a wide variety of educational programs aimed at youth and adults, it is not known which methods are most effective in preventing the start of smoking or in

lowering tar and nicotine in cigarette smoke (*49*), and major efforts undertaken in the research sector to develop and evaluate a less hazardous cigarette (*24*), the interactions between the physical/chemical characteristics of the cigarette and the behavioral/physiological characteristics of the smoker are being given increasing attention.

As discussed elsewhere in this report, there are many theories about why people smoke. While in most cases the explanation is not simple, nicotine is a generally agreed-upon factor. Nicotine has long been considered as habitual at least and, by some persons, as an addictive drug (*22, 37, 54*). The Third Report of the Royal College of Physicians of London (1977) is quite explicit in stating that "Tobacco smoking is a form of drug dependence different from but no less strong than that in other drugs of addiction" (*50a*). The pharmacodynamic implications of smoking have generated detoxification techniques in smoking-cessation programs, the search for nicotine substitutes or anticotine drugs (e.g., lobeline (*26*)), the presentation of nicotine in an alternate vehicle (e.g., chewing gum (*52*)), and the evaluation of nicotine aerosol techniques in terms of their impact on modifying smoking behavior (*28*).

Because of the role of nicotine in creating a dependency for the smoker, it is appropriate to consider smoking patterns and the effects these patterns have on response to cigarette smoke components. There are many ways to characterize smoking patterns:

Type of cigarette smoked. Cigarette brands vary radically today in terms of nicotine and tar delivery and somewhat less in terms of CO, acrolein, HCN and NO_x's

Number of cigarettes smoked. This ranges from none to a maximum of about 100 cigarettes a day

Amount of cigarette smoked. Smoking patterns range from smoking only the first few millimeters to smoking down to a few millimeters from the butt end. Inasmuch as the tobacco at the butt end of the cigarette acts as a filter and builds up nicotine and tar as the cigarette is smoked, the last few puffs on a cigarette smoked all the way down will have a much higher nicotine and tar delivery than the first puffs.

Number of puffs. This can range from one or two puffs up to about 20

Depth of inhalation. Again, this can vary from the pattern of the noninhaler to deep inhalation.

Length of inhalation. The longer the cigarette smoke is held in the lungs, the greater the absorption and thus, the deposition of smoke.

Since it would be possible for an individual smoking 10 cigarettes per day to absorb more of the components of cigarette smoke than one who smoked many times that number, realistic evaluation of smoking impact calls for the development of dosimetric techniques applicable to research, screening, and smoking-pattern modification programs.

TABLE 21.—Relative molar potency of nicotine and other cigarette smoke alkaloids

Alkaloid	Concentration of fumes at pH neutr.	Flavor action in packed rat	Release of catecholamines from cat adrenal	Contraction of frog rectus	Bioassay of contraction of guinea pig duodenum	Inhibition of cat liver perf.	Inhibitor of cat flexor reflex	Inhibition of cat flexor reflex	Inhibition of brain enzyme extractor reflex
Nicotine	100	100	100	100	100	100	100	100	100
Nornicotine	45	28	56	61	73	56	56	36	47
Metanicotine	4	3	-	-	0.8	0.4	0.6	0.6	1.25
Anabasine	17.5	80	72	88	50	17	80	80	80
Anatabine	0.2	5.5	-	3	12	3	3	1.3	3
Myosmine	0.2	2.5	-	0.4	17	17	5.1	5.1	10
Dihydrometanicotine	0.05	0.5	-	-	0.08	0.4	0.6	0.6	-
2,3-Dipyridyl	0.2	-	-	-	4	0.1	0.1	-	-
Cotinine	0.001	0.1	0.03	-	0.8	0.06	0.5	-	-
Nicotyrine	0.025	2	-	-	0.9	-	-	-	-

SOURCE: CHEK, M.S.G. (*12*)

As might be expected, the smoking pattern affects absorption of the content of cigarette smoke, and consequently the toxic effects, differentially. Some of the contents and characteristics of the smoke also modify smoking patterns.

Since nicotine is absorbed through the mucus membranes and the skin as well as the alveoli, it will be absorbed, to a lesser degree, even by the nonInhaler. (The nicotine from snuff and chewing tobacco is absorbed only through the mucus membrane route as is the case for most nonInhaling cigar smokers.) Although the absorption of nicotine is to some degree independent of smoking patterns, there is significant evidence, not uniformly accepted, that a number of dimensions of smoking patterns are to a large degree dependent on nicotine content of the cigarette. Increasing evidence indicates that chronic "nicotine-dependent" smokers tend to titrate or compensate their inhalation profile in order to develop a desirable blood level of nicotine (*41*). This is done by modifying the number of cigarettes smoked, the number of puffs, the amount of cigarette smoked, or the depth of inhalation (*9, 39*). The implication of this apparent compensatory modification of smoking pattern to assure a preestablished nicotine titration level in the smoker has broad ramifications when considered in the context of the increasingly popular lower-nicotine cigarettes designed to give low delivery. Since this is an area to which major attention has been devoted only recently, a serious research effort should be mounted in order to better understand this "titration" phenomenon. The implications for differential tax sanctions based upon nicotine delivery, as well as for the direction of development of less hazardous cigarettes, need exploration in depth. Since the pH of the urine affects the rate of elimination of nicotine from the blood stream, it might be expected to have an impact on the nicotine titration process with accompanying modification of smoking patterns (*53*), hence it should also be examined in greater detail.

Another characteristic of cigarette smoke which modifies smoking patterns is the pH (*9*). As has been mentioned earlier, cigarette smoke of the bright type or U.S. blending formula is mildly acidic, which results in relatively little irritation to the mucosa as compared to mildly basic smoke, and can accordingly be inhaled without unpleasant effects by many smokers. Cigar smoke, on the other hand, is mildly basic and is quite irritating to the mucosal tissues, for this reason, cigar smokers are less apt to inhale, or to inhale deeply, than are cigarette smokers. It has also been suggested that cigars are satisfying without being inhaled.

The remaining major toxic elements of cigarette smoke (CO and NO_x's) are absorbed primarily through the alveoli (acrolein and HCN are water soluble gases and are readily absorbed in the upper respiratory tract), and accordingly the inhalation characteristics of the smoker will have a direct impact on the short- and long-range effects of these substances. Further, the ciliatoxic effects of HCN and the ciliastatic effects of acrolein will depend to a major extent on the inhalation pattern of the smoker. Lastly, the contribution of the NO_x's to chronic obstructive pulmonary disease depends to a major extent on the presentation of these substances at the alveolar site; as a result, inhalation practices will strongly affect the pathological sequelae of the NO_x compounds.

Thus, the consequences of cigarette smoking would appear to be dependent not only on the composition of the smoke itself, but also on the smoking patterns of the individual smoker. More extensive effort is needed to develop dosimetric and puff-analysis tools and techniques as a basis for better understanding of the pharmacokinetic and smoking behavioral dimensions of cigarette smoking.

Summary

The smoking of a cigarette seems to satisfy a smoker's physiological and psychological needs, and it is generally accepted that nicotine is the principal constituent responsible for cigarette smokers' pharmacologic responses.

Nicotine is rapidly absorbed in both the oral cavity and lungs, especially at basic pH. It is a quick-acting ganglionic stimulant on both the sympathetic and parasympathetic ganglia.

Nicotine causes the release of catecholamines, epinephrine, and norepinephrine. Several physiological responses have been attributed to nicotine and/or catecholamines, such as increased heart rate and blood pressure, cardiac output, stroke volume, velocity of contraction, myocardial contractile force, oxygen consumption, coronary blood flow and arrythmias, bronchoconstriction and related pulmonary manifestations, increased mobilization and utilization of free fatty acids, hyperglycemic effects, and a decreased patellar reflex response.

Considering the nicotine metabolites in cigarette smoke and the presence of minor amounts of related alkaloids, nicotine exerts the strongest response in a variety of biochemical and physiological tests.

Considerable evidence exists, although it is not uniformly accepted, that smoking patterns of chronic smokers are dependent on the nicotine content of the cigarette and dependent on what the nicotine delivery would be when measured by the standard methodology. Smoking patterns are dependent, to varying degrees, on the type of cigarette smoked, the number of cigarettes smoked, the length of the cigarette rod burned, the number of puffs, the depth of inhalation, and the length of inhalation. Nicotine absorption is also dependent on the above-mentioned parameters as well as on urine pH, which affects the rate of elimination of unmetabolized nicotine.

TABLE 1.—Cigarette smoke: gas phase components (μg/cigarette*)

Carbon monoxide	13 400
Carbon dioxide	50 600
Ammonia	80
Hydrogen cyanide (hydrocyanic acid)**	240
Isoprene (2 Me 1,3 butadiene)	582
Acetaldehyde	730
Acrolein (2 propenal)	84
Toluene	108
N Nitrosodimethylamine	0 08
N Nitrosomethylethylamine	0 03
Hydrazine	0 03
Nitromethane	0 5
Nitroethane	1 1
Nitrobenzene	25
Acetone	570
Benzene	67

* 85 mm non filter, blended cigarette (U S)
** Gas phase portion only (74 μg rig. in particulate phase)
SOURCE Schmeltz I (114)

TABLE 2.—Cigarette smoke: particulate phase components (μg/cigarette)

TPM* wet	31,500
dry	27,900
FTC**	26,100
Nicotine	1 800
Phenol	86 4
o Cresol	20 4
m and p Cresol	49 5
2,4 Dimethylphenol	9 0
p Ethylphenol	18 2
β Naphthylamine	0 0.28
N Nitrosonornicotine	0 14
Carbazole	1 0
N Methylcarbazole	0 23
Indole	14
N Methylindole	0 42
Benz(a)anthracene	0 064
Benzo(a)pyrene	0 025
Fluorene	0 42
Fluoranthene	0 26
Chrysene	0 04
DDD	1 75
DDT	0 77
4,4 Dichlorostilbene	1 73

* U S cigarette, 85 mm without filter tip 1968
** TPM FTC = TPM (#s) nicotine
SOURCE Schmeltz I (114)

Carbon Monoxide

After nicotine, the substance in cigarette smoke with the most pronounced acute pharmacological action is carbon monoxide (CO). Cigarette smoke contains 1 to 5 percent CO, or 10,000 to 50,000 parts per million (ppm). Carbon monoxide impairs the oxygen-carrying capacity of the blood and may impair functioning of the nervous system. It appears to pose a threat, both acutely and chronically, to the functioning of those with cardiovascular disease. Indeed, it is thought by some (*128*) that the carbon monoxide in cigarette smoke is partially responsible for the increased risk of myocardial infarction and stroke in cigarette smokers. The combination of nicotine, with its catecholamine releasing properties, and carbon monoxide in the blood of smokers may enhance cardiovascular risk.

Little evidence exists to support the hypothesis that carbon monoxide is the reinforcing agent in establishing the smoking habit, although it may interact with nicotine. Quite possibly carbon monoxide may deter a few smokers from establishing the smoking habit because it may induce headaches which would deter further smoking. Other forms of tobacco (snuff and chewing tobacco) that have been used through the ages do not produce carbon monoxide.

Tar

Tar, the particulate phase of cigarette smoke, is also of importance in the establishment of the smoking habit. The possibility that tar may be reinforcing is not so easily disproved because the tar and nicotine content of cigarettes tend to co-vary. One study in which the tar and nicotine were dissociated and varied (*38*) showed that the number of cigarettes smoked was related to the nicotine content but not to the tar. There were indications that there may be an interaction between tar and nicotine. For example, nicotine strongly influenced strength ratings in the expected direction, while high tar cigarettes were actually perceived as milder than low tar. The results are consistent with the hypothesis that people smoke to obtain nicotine, but it would be important to extend and confirm these findings with a wider range of tar and nicotine content.

Nicotine

Nicotine has been proposed as the primary incentive in smoking (*63*) and may be instrumental in the establishment of the smoking habit. Whether or not it is the only reinforcing agent, it is still the most powerful pharmacological agent in cigarette smoke. Nicotine is rapidly extracted, enters the pulmonary circulation, is pumped to the aorta where it stimulates the aortic and carotid chemoreceptors, and may produce reflex stimulation of the respiratory and cardiovascular centers in the brain stem.

Within one circulation period, one fourth of the inhaled nicotine passes through the brain capillaries and, since it is highly permeable to the blood brain barrier (*99*), passes promptly into the brain. Once in the

brain, nicotine stimulates nicotinic receptors. It also releases various biogenic amines, including the catecholamines and possibly 5-hydroxytryptamine. It may also stimulate some as yet unidentified receptors. It stimulates the emetic chemoreceptor trigger zone in the medulla and, in novices or in large doses, it causes nausea and vomiting. A variety of hypothalamic and pituitary hormones are stimulated by nicotine (*143*). The effects of nicotine on associative centers in the brain are still unexplored but may be of extreme importance in explaining its use and desirability during initiation of the smoking habit. Studies from a number of laboratories indicate that nicotine can have a facilitating effect upon learning and memory in animals (*84*), and possibly in humans (*2*).

The other three-fourths of the inhaled nicotine is delivered to the rest of the body and acts wherever there are nicotinic sites. Thus it stimulates autonomic ganglia with, for example, activation of the gastrointestinal tract. By the same mechanism, it releases epinephrine from the adrenal gland with all the "fight or flight" reactions that this hormone can produce, including mydriasis, tachycardia, vasoconstriction, bronchiolar dilitation, decrease in gastrointestinal motility (though this is generally successfully overcome by nicotinic ganglionic stimulation), and glycogenolysis. It also produces a rise in free fatty acids in the blood, and it can release catecholamines such as norepinephrine from nerve endings and chromaffin cells through the body. These diffuse physiological changes may contribute to increased arousal and thus be important corollaries in the establishment of the smoking habit.

Much of the evidence for the role of nicotine as the primary reinforcer in cigarette smoke is circumstantial. Smokers prefer cigarettes with nicotine than without (*40*), though they will smoke nicotine-free cigarettes.

Cigarettes with a nicotine content of less than 0.3 mg/cig do not do well on the market but recently have been increasing in popularity. Generally, these are smoked by individuals who are trying to cut down or somehow diminish the harmful effects of smoking. Tobacco-free cigarettes are doomed to oblivion almost from the start. Lettuce cigarettes had a brief vogue in the United States, but the two companies producing the two different brands on the market went bankrupt.

It is important to note that low or no-nicotine cigarettes allow their smokers to go through all the motions of smoking. Lighting, handling, and puffing can be the same as with usual cigarettes, so the opportunity for visual, olfactory, and oral gratification is present. It is the rare smoker, however, who continues to smoke cigarettes lacking nicotine for any length of time when the more popular high nicotine cigarettes are available. The most likely explanation for this preference is that nicotine is reinforcing.

Metabolism and Fate of Tobacco in the Body

There is little data relating metabolism and fate of tobacco to the establishment of the smoking habit in adolescence. Differences, however, have been found in the metabolism of tobacco in adult nonsmokers and smokers. Beckett and Triggs (*8*) administered nicotine to smokers and nonsmokers and measured urinary nicotine content. The nicotine content in urine from smokers (55 to 70 percent) was consistently higher than from nonsmokers (25 to 50 percent). It would be useful to do enzyme studies in a large sample of adolescent and preadolescent subjects to determine whether chemical profiles might help predict who will take up smoking and who will not. Also, if there are biological deterrents to smoking, it would be useful to find them.

Predisposing Factors

Genetic

Relatively little is known about biological factors in the initiation of the smoking habit. Many studies that have implicated biological factors in the initiation of smoking behavior attribute the behavior to a genetic predisposition. Initial twin studies by R. A. Fisher (*33*) led him to hypothesize that genotype was a significant variable in smoking behavior. In his survey of twins from Germany and England, he reported that monozygotic twins were more concordant in their smoking behavior than dizygotic twins.

Eysenck (*30*) has measured personality variables and has concluded that smoking behavior is related to the extroversion-introversion dimensions of personality. Eysenck's theory assumes that differences in these dimensions of personality are for the most part determined by hereditary factors. He presents evidence indicating that monozygotic twins are more alike on these dimensions than dizygotic twins, and that cigarette smoking is associated with the extroversion dimension of personality. These data have in part formed the basis for the common genotype hypothesis. This hypothesis states that tobacco smoking and lung cancer (and in the theory of Eysenck, personality factors) are due to a common genetic mechanism (*76*). Subsequent analysis of twin studies have supported (*18, 119*) and denied (*113, 139*) a significant genetic influence on smoking behavior. However, Cederlof, et al. (*19*) recently published an extensive review of the data from the Swedish twin registry and concluded that "the constitutional hypothesis as advanced by Fisher and still supported by a few, has here been tested in twin studies. The results from the Swedish monozygotic twin series speak strongly against this constitutional hypothesis." The Chapter on Mortality in this report contains a more complete discussion of this topic.

In general, studies from which inferences about genetic mechanisms and smoking have been made are subject to many of the pitfalls

associated with survey-type research. Studies of twins are among the most popular means of assessing genetic factors (*14*). Unfortunately, the small number of subjects used in twin studies (particularly monozygotic) has limited the inferences that can be made about genetic mechanisms. An additional confounder not controlled in twin studies is the prenatal environment. The prenatal environment for monozygotic twins is likely to be more similar (i.e., twin positions, common circulatory factors, etc.) than for dizygotic twins (*88*). Further progress in this area will depend on more exhaustive and sophisticated methods of analysis.

Endocrinological

The importance of endocrine factors in the establishment of the smoking habit has not been explored. There is abundant evidence that hormonal changes in puberty occur at about the same time that individuals start smoking. Retrospective studies indicate that teenage smokers are more outgoing, self-confident, and rebellious toward established authority than their nonsmoking counterparts.

The acute endocrine changes associated with cigarette smoking are difficult to interpret because of non-specific stress factors which may accompany smoking. Winternitz and Quillen (*149*) measured ACTH and growth hormone levels in nonsmokers after smoking two cigarettes. There was a rapid increase in the plasma levels of both hormones, but the authors were unable to determine if the effect was due to the tobacco smoke or to the stress created by smoking. The subjects developed nausea, became pale, and started sweating. In chronic smokers a sharp rise in plasma cortisol was observed after two cigarettes and was maintained for several hours. Growth hormone levels peaked at 1 hour and fell back to control levels during the second hour of measurement. No significant changes were found in LH, FSH, TRH, and testosterone levels.

One of the most frequently demonstrated endocrine effects of nicotine is the stimulation of vasopressin release from the supraoptic nucleus (*5, 46, 110*). Robinson and his colleagues have shown in humans that nicotine stimulates the release of a neurophysin associated with vasopressin secretion. A second estrogen-stimulated neurophysin was not affected by nicotine treatment.

In a similar study, Hayward and Pavasuthipaisit (*46*) measured plasma vasopressin levels in adult female monkeys after intravenous infusion of nicotine (100 μg/kg/min). A significant increase in circulating vaspressin levels was measured that could, in part, be abolished by pre-treatment with promethazine and diphenhydramine. The association between endocrinological responses and smoking is not clear, however. That smoking *causes* such responses has been established, but it would be important to determine whether these responses in turn reinforce further smoking.

Acute Effects of Tobacco and Its Constituents Upon Establishment of Smoking

Central Nervous System

It is clear that tobacco has reinforcing properties that motivate its users to continue smoking even when they are aware of the possible health consequences. Nicotine appears to be the chemical in tobacco that is most likely responsible for these effects (*63*). When the nicotine and tar content are varied independently, it is the nicotine content that is correlated with ratings of strength and satisfaction (*39*). Numerous investigators have shown that nicotine will release norepinephrine from postganglionic sympathetic sites, acetylcholine from postganglionic parasympathetic sites, and epinephrine from the adrenal medulla. However, the primary sites of reinforcement appear to be in the central nervous system. Oldendorf (*99*) has demonstrated that nicotine readily crosses the blood-brain barrier. Stolerman, et al. (*127*) administered mecamylamine, a central nicotine antagonist, to smokers and observed an increase in cigarette consumption. This change was presumably an attempt to overcome the blockade. Further, when the peripheral antagonist, pentolinium, was administered, no change in cigarette consumption was noted. These data are supported by animal studies indicating that rats trained to discriminate nicotine from saline do not generalize the response to similar drugs (*116*). In a related study, Hirschhorn and Roserans (*51*) reported that mecamylamine abolished an established nicotine discriminative response.

An important central nervous system effect of nicotine is its ability to modulate arousal levels. The cortical EEG has been used by many investigators as an index of changes in arousal processes (*58, 66, 135*). When smokers are deprived of tobacco for short periods of time, there is an increase in lower-frequency and high-amplitude waveforms in their EEG, thus indicating a possible state of "hypoarousal." Interpretation of these studies has proved difficult because adequate control groups were not employed. It is possible that the process of inhaling in a manner that simulates smoking will elicit the same EEG changes as smoking a cigarette.

The study of Kales, et al. (*66*) in some ways tempers this criticism in that it demonstrated differences in sleep patterns between nondeprived and deprived smoking conditions. During deprivation, smokers spent more time in REM sleep than during nondeprived states. This result could also be due to nonspecific stress.

Research has shown that animals may self-administer nicotine. For example, Pradhan and Bowling (*106*) studied the effects of intraperitoneal administration of nicotine on self-stimulation in rats. The baseline rate of self-stimulation varied as a function of electrode placement, current intensities, and time spent lever-pressing. At high baseline levels of self-stimulation, nicotine enhanced the rate of stimulation.

These data are consistent with other studies that demonstrate that drug effects are largely dependent upon baseline levels of self-stimulation. In a somewhat different approach, Yanagita (*153*) has studied the reinforcing properties of nicotine by demonstrating that monkeys will self administer nicotine on a regular basis when given the opportunity. An earlier study by Deneau and Inoki (*23*) presented similar results.

There are very few studies in which nicotine alone has been administered to man in an attempt to produce reinforcement (*64, 65, 80*). Johnston injected himself and other volunteers with nicotine and obtained clear evidence of reinforcement. These unique studies were uncontrolled for suggestion, however. There were three studies in which nicotine was given either by ingestion or intravenously, and in all three, it was incapable of completely suppressing smoking, though it usually had some suppressant effect. Indeed, in the experiment by Kumar, et al. (*75*), there was no discernible effect of a rapid intravenous infusion of 1.17 mg of nicotine. Subjects went on puffing their cigarettes just as they did with an equivalent injection of placebo, and there was no delay in latency to the first puff.

The results are disturbing to proponents of the nicotine hypothesis of smoking. It is clear that the intravenous infusions had no effect on the subsequent puffing of cigarettes, whereas the cigarettes smoked immediately preceding the test session had a marked effect both on latency to the first puff and on the rate and volume of puffing. Perhaps the nicotine delivered to the blood and brain were not equivalent in the two conditions. Perhaps the intravenous dose should have been higher, it might have been swamped by the fact that *ad lib* smoking was allowed during the intravenous administration of nicotine. Clearly more research is needed to clarify these results.

If it could be established that central nervous system effects of smoking were reinforcing, it would be important to study these actions in novices.

Cardiovascular System

Before he takes his first cigarette, the novice is not likely to be aware of his cardiovascular system. The first cigarette, however, may have a very profound effect upon the heart and blood vessels of a nonsmoker. The tachycardia may be perceived either as a pleasant or unpleasant sensation. The cardiovascular changes associated with tobacco intake resemble the effects elicited by nicotine alone. Both sympathetic and parasympathetic ganglia are stimulated by low concentrations of nicotine, and nicotine can have sympathomimetic effects by releasing epinephrine and norepinephrine from chromaffin cells in the adrenal medulla, heart, blood vessels, and skin (*139*). Increases in heart rate (10 to 25 beats per minute), blood pressure (10 to 20 mm Hg systolic, 5 to 15 mm Hg diastolic) and cardiac output (0.5 l/min/m^2) typically occur in both nonsmokers and smokers after smoking one or two cigarettes. In addition, digital blood flow and finger and toe temperature fall (*139, 151*).

The acute cardiovascular responses to tobacco and nicotine have been summarized in the Surgeon General's reports on the health consequences of smoking (*136, 138*). These reports list the following acute changes from smoking: increased (1) heart rate, (2) blood pressure, (3) cardiac output, (4) stroke volume, (5) velocity of contraction of the heart, (6) myocardial contractile force, (7) coronary blood flow, (8) myocardial oxygen consumption, (9) arrhythmia induction, and (10) electrocardiographic changes. These effects are assumed to be due to catecholamine release from the adrenal medulla, chromaffin tissue, or sympathetic nerve endings, and are similar to those obtained by sympathetic stimulation. They are to a considerable extent mediated by sympathetic excitation (*139*). These diverse cardiovascular changes may be a significant component in shifting the arousal continuum toward an optimum level for smokers. However, there are no controlled experiments that definitely rule them in or out as contributors to the reinforcing properties of cigarettes.

Maintenance of the Smoking Habit

The biological factors which can be implicated in the maintenance of smoking have, by no means, been thoroughly investigated. A great deal is known about the *harmful* biological consequences of smoking, but very little about the *beneficial* effects. It is evident that some component or components in tobacco and tobacco smoke must be reinforcing, but these have not been unequivocally identified. As noted earlier, the possible candidates for reinforcing agents can be seen in the two tables (Tables 1 and 2) from Schmeltz and Hoffman (*118*). The leading contender is nicotine because it is clearly a powerful pharmacological substance and is administered in ways consistent with its action as a reinforcer. There are, however, some inconsistencies in the literature. Yanagita (*153*) has reported low levels of nicotine self-administration in monkeys and rats respectively, while Russell, et al. (*111*) report a lack of evidence for self-administration in man, as well as in other animals. The present discussion focuses upon tolerance to tobacco and its constituents, the metabolism and fate of the constituents, and their physiological effects as they relate to the maintenance of the smoking habit.

Tolerance

By definition, tolerance is manifested by a decreasing response to repeated administration of the same dose of a drug, or by the requirement for increasing doses in order to elicit the same response. Martin (*81*), Jaffe and Sharpless (*61*), and others have proposed models

which imply that dependence and tolerance are based upon identical mechanisms. It is difficult to think of an example of a drug to which dependence occurs that does not also involve tolerance. On the other hand, tolerance may occur without dependence (e.g., phenothiazine, antihistamines).

Three kinds of tolerance are apt to occur with tobacco use as with other types of drug use: drug dispositional or metabolic tolerance, tissue or pharmacodynamic tolerance, and behavioral tolerance. The first refers to methods that the body uses to eliminate or to deactivate the drug. For most chemicals derived from tobacco, the liver is the organ most heavily responsible for detoxifying or transforming them into inactive and eliminable forms. The kidney is also important, especially for alkaloids whose water solubility varies with the pH of the solution. The second kind of tolerance refers to changes in the ability of receptors to be activated by the drug at its final site of action. The third type refers to the way in which the subject using the drug changes his behavior to adapt to the effects which the drug repeatedly produces.

Of the compounds contained in tobacco and tobacco smoke (*118*), three are of primary biological importance: tar, carbon monoxide, and nicotine. There is evidence that tolerance can develop to the effects of each of these, although their interaction has scarcely been studied. While there is evidence that tolerance may develop to other components such as acetone and phenol, it is unclear how much they contribute to the pharmacological actions of cigarettes.

Nicotine

Stolerman, et al. (*126*) examined the interaction between pairs of injections of nicotine which varied both in dose and in interval. Two measures of spontaneous locomotor activity of rats in a T-maze were taken: rears and entries. After a single treatment with nicotine, acute tolerance developed as indicated by a shift of the dose-response curve. The dose of nicotine required to produce a given decrement in activity was multiplied by a factor of about 2.4 when a delay of 2 hours was taken between the two injections. When the initial dose was varied, it was found that there was an optimal level for producing tolerance. Higher doses were less effective. An explanation for the relative ineffectiveness of the higher doses in producing tolerance is not available. A general debilitating effect of pretreatment with large doses does not seem to explain it, as rats given a saline challenge exhibited normal motor activity. Perhaps the debilitating effects of a large pretreatment dose and a challenge somehow summate.

Carbon Monoxide

Levels of carbon monoxide achieved in the human body following cigarette smoking increase levels of carboxyhemoglobin. These chronically high levels of carboxyhemoglobin found in smokers can induce polycythemia by increasing hemoglobin levels. These compensatory changes enable the smoker to tolerate increased carbon monoxide levels and to cope with the oxygen deficit produced by cigarettes.

Tar

Tar is defined as the total particulate matter (TPM) collected by a Cambridge filter after subtracting moisture and nicotine. The polycyclic aromatic hydrocarbons are generally blamed for a substantial portion of the carcinogenic activity of tar. They are also powerful enzyme inducers and are undoubtedly responsible for much of the tolerance to themselves and a variety of other compounds produced by smoking. The tar content of cigarette smoke for all brands is determined yearly by the Federal Trade Commission which publishes a listing, along with nicotine content. Tar and nicotine tend to co-vary and thus their effects may be confounded. Obviously, tar is obtained in the smoke from pipes and cigars but not from chewing tobacco and snuff. The latter do not deliver pyrolysis products, such as carbon monoxide, and may thus be somewhat safer. Because the hepatic microsomal enzyme formation is induced by a number of carcinogens in the tar fraction of cigarette smoke, including benzopyrene (*96*), smokers are rendered tolerant to both the therapeutic and toxic effects of a wide variety of drugs (*129*). Even the enzymes in platelets are activated (*53*).

The phenomenon of tolerance to the effects of tobacco products has been clearly demonstrated in both humans and animals. As might be expected, most of the emphasis has focused upon nicotine, but carbon monoxide and tar components also play an important role. As with all other drugs, tolerance varies with subjects and functions. Certain invertebrate forms which feed on the tobacco plant have a high genetically determined tolerance. It is reasonable to assume that even in humans some of the variance in response to tobacco is innately determined and may account for some of the high concordance in smoking behavior seen in identical twins. Other forms of tolerance are clearly the result of experience and develop after exposure to tobacco products. Much more research needs to be done to determine the degree of tolerance which develops in different physiological and psychological functions after tobacco use. For example, it is evident that even in heavy smokers of long duration the heart rate speeds up after each cigarette. On the other hand, nausea and vomiting diminish and disappear with continuing moderate use of cigarettes. It would be very informative indeed to know what changes take place at the

putative sites of action of nicotine with chronic use. Do nicotinic synapses at ganglia change in the same way as nicotinic synapses in the brain? Do carbon monoxide and tar constituents have any action on these components or on enzyme systems elsewhere in the body? Answers to these questions will enable us to understand better the physiological basis of the smoking habit.

Tolerance to the effects of cigarette smoke was noted in dogs given cigarette smoke via tracheostomy (*44*). At the beginning of the study the smoke was aversive, but with the passage of time, animals exhibited tail wagging and improved cooperation. In a careful study, Stolerman, et al. (*127*) showed the development of both acute and chronic tolerance in rats. Nicotine administered intraperitoneally to experimentally naive rats depressed activity in a Y-shaped runway in a dose-related manner. After a single intraperitoneal dose of nicotine, acute tolerance to the depressant action of a second dose developed with a definite time course. This became maximal after 2 hours and wore off after about 8 hours. Repeated intraperitoneal doses of nicotine (three times daily for 8 days) elicited chronic tolerance which persisted for at least 90 days after the end of regular treatment with the drug. Tolerance was also produced when nicotine was administered in rats' drinking water and through reservoirs implanted subcutaneously. It appears, then, that tolerance to nicotine in rats can develop quickly, may be easily measured, and persists for prolonged periods after withdrawal. In these experiments, rapid withdrawal of nicotine did not produce the signs of illness which morphine withdrawal regularly produced. The existence of prolonged tolerance to nicotine in rats suggests that the same phenomenon might exist in man. If tolerance to the unpleasant effects of nicotine, such as nausea, developed more rapidly and persisted longer, it might facilitate relapse to tobacco use.

Metabolism

Nicotine

The metabolic fate of 1 mg of nicotine base injected intravenously in humans (actually as nicotine hydrogen tartrate) was intensively investigated by Beckett, et al. (*7*). They found that smokers excrete nicotine significantly faster than nonsmokers. None of the smokers reported any nausea from the nicotine injections, but this was reported in varying degrees by all nonsmokers. Haines, et al. (*42*) reported that the plasma concentrations of nicotine were actually higher in smokers than in nonsmokers 1 minute after smoking, but these results were confounded by the fact that nonsmokers were instructed to smoke cigarettes. Obviously smokers were able to inhale more effectively than nonsmokers, in part because they had acquired tolerance to the aversive effects of cigarette smoke on the respiratory passages. Indeed, some of the tolerance that smokers show to cigarette smoke

may be correlated with diminished function of the respiratory epithelium and possible depression of taste and smell (*70*). The proposition that heavy smokers adjust their plasma nicotine levels is compatible with the observation that regular smokers commonly consume about 20 to 30 cigarettes during the smoking day (approximately one every 30 to 40 minutes) and that the biological half life of nicotine in humans is approximately 20 to 30 minutes (*57, 111*). While studies with intravenous nicotine (*80*) show changes in smoking rate apparently due to nicotine concentration in the blood, studies using nicotine gum (*73*) did not show the same effects as intravenous nicotine. It is postulated that the nicotine derived from the gum is absorbed in the intestine and sent to the liver directly via the portal and is there metabolized; therefore less nicotine enters the systemic circulation. Most investigations of smoking rates indicate that much more than plasma nicotine level regulation is involved.

Carbon Monoxide

The metabolism of carbon monoxide involves both the exhalation of the substance from the lungs and a compensatory increased hematocrit to increase oxygen capacity. The former is slowed by the high affinity of carbon monoxide for hemoglobin, and the latter's rate is limited by the process of hematopoiesis. Carboxyhemoglobin has a half life in the body of at least 3 to 4 hours (*137*). It is not known whether the metabolism of carbon monoxide plays a physiological role in the maintenance of the smoking habit.

Tar

Some examples of the effects of induction of microsomal enzymes are cited by Hunter and Chasseaud (*54*). Aryl hydrocarbon hydroxylase is regularly induced by smoking. Benzopyrene hydroxylase and aminozao dye N-methylase were higher in the placentae of pregnant smoking women than in those of nonsmokers. Since tar induces the enzymes of its own metabolism, the smokers might be expected to continue to smoke so as to maintain the levels of tar in the blood, thereby maintaining the action of tar on the metabolism of toxic substances, as discussed above. Metabolism of benzodiazepines, propoxyphene, pentazocine and phenacetin is increased in smokers. Xanthines such as theophylline are also metabolized more quickly in smokers (*105*) and, by inference, so should caffeine be metabolized more quickly. Perhaps this is why heavy smokers drink more coffee than nonsmokers (*9*).

Dependence

Dependence may play an extremely important biological role in the maintenance of the smoking habit (*147*). The characterization of tobacco use as a dependence process raises the issue of tobacco

withdrawal. Thus, the subject of dependence is deferred to the section on cessation of the smoking habit to be discussed in conjunction with the acute effects of cessation and the abstinence syndrome.

Physiological Effects of Tobacco and Its Constituents in the Maintenance of Smoking

Although a great deal has been written in previous editions of the Surgeon General's Report on the untoward effects of smoking, very little has been said about the factors that might be responsible for the establishment and maintenance of the habit. In the past 15 years the public has been exposed to ample warnings about the dangers of smoking, nonetheless the incidence of smoking remains high. Therefore, it is important to consider both the evidence and hypotheses about why smoking is such a tenacious habit. The actions of cigarette smoke and its components upon the central nervous system, cardiovascular system, and endocrine system might give us a clue to the strength and persistence of the habit.

Central Nervous System

In their study of smokers, deprived smokers, and nonsmokers, Knott and Venables (*72*) showed that the deprived smoker is characterized by a "state of cortical hypo-excitation and that tobacco smoking increased cortical excitation to the level of the nonsmoker." Citing the findings that tobacco smoking improves efficiency, prevents deterioration of reaction time (*35*), and improves learning (*1, 3, 17*), they suggest "that individuals smoke to achieve this specific psychological state of increased vigilance and attention associated with alpha frequency."

Nelsen, et al. (*95*) studied the effects of nicotine administered (100 μg/kg) subcutaneously to rats. The rats had electrodes placed in the reticular formation which, when stimulated, blocked visual learning tasks. The nicotine attenuated the electrical stimulation and increased learning. The suggestion is made that the nicotine-induced limbic system activation antagonized the behavioral disruption.

In Carruthers' attempt to isolate the "rewarding centers" (*16*), he used a β-blocker, oxprenolol, to decrease epinephrine and norepinephrine associated with anxiety and smoking. The secondary effects of increased heart rate, blood pressure, and free fatty acids were blocked along with the systemic increase in catecholamines, and yet the satisfaction subjectively evaluated was unchanged. His conclusion was that there may be a hypothalamic norepinephrine release leading to pleasure. It is not clear whether the oxprenolol crosses the blood-brain barrier. The more conservative conclusion would be that heart rate, blood pressure, and free fatty acid increases might not be involved in the pleasure associated with smoking.

In addition to the learning studies mentioned above, recent studies add the following data. Stevens (*124*) studied 115 males on four learning tasks. His conclusion was that those who smoked more than 12 cigarettes per day did significantly less well than the nonsmokers and light smokers. Andersson and Hockey (*2*) showed that, in two groups of 24 female students who were habitual smokers, the group in a control, no-smoking condition showed immediate serial recall equivalent to that of the group allowed to smoke one cigarette. The group not smoking did perform better in incidental memory, such as remembering in which corner the words were presented. This suggested that the cigarette increased attentional selectivity during increased arousal. Elgerot (*28*) used three complex and two simple tests to determine differences between a 15-hour abstaining group and the same group after smoking freely. In the nonsmoking condition, they improved on complex tests but were unchanged with respect to simple tests. The interpretation is based on the performance-arousal curve: "According to the Yerkes-Dodson law, the optimal level for arousal is lower for complex than for simpler tests." The conclusion is that the combination of the task and the cigarette led to an arousal level too great for the complex tests. An alternative hypothesis is that the smokers were under-aroused and that the abstainers were anxious enough, but not too anxious. The second explanation would account for the finding, but it is not consistent with other authors. Elgerot (*28*) cites the following effects in habitual smokers: (1) decreased hand-steadiness (*36*), (2) improved simple and choice reaction times (*93*), (3) improved driving tasks demanding sustained performance (*48*), and (4) impaired short-term memory but favorable effects on consolidation (*1*). Some of these changes in arousal levels and functioning capacities may be of benefit to the smoker and may reinforce maintenance of the smoking habit.

Other effects of smoking on the nervous system may be positively reinforcing. Decreased acetylcholine axonal transport and synthesis in neurons (*49*) may lead to decreased GI motility and augment the sympathetic response in calming digestion. Other investigators have shown no basic differences in the basic taste sensations between smokers and nonsmokers (*83*).

Cardiovascular System

The most commonly reported acute changes in the cardiovascular system are the following: increase in plasma catecholamines (*4, 78*), increased heart rate (*4, 5, 78*), increased blood pressure (*4, 5*), vasoconstriction (*43, 94*), and increased carboxyhemoglobin (*4, 98*). It is conceivable that cardiovascular changes are associated with pleasant emotional experiences, although Carruther's (*16*) β-blocking experiment would not support this possibility. Possibly decreased peripheral blood flow (*43*) is a heat-conserving mechanism which may drive

individuals to smoke. The increased viscosity of the blood due to increased hematocrit (*140*) is of unknown benefit on a chronic basis.

Endocrinological System

Although there has been much recent research on endocrine effects of smoking, the role these play in the smoking habit has scarcely been examined. With the development of more refined and more economical techniques for measuring hormones and their actions, we can expect an acceleration of research in this area.

Hayward and Pavasuthipaisit (*46*) administered IV nicotine to monkeys, causing an increase of arginine vasopressin (AVP) without changes in plasma osmolarity. Husain, et al. (*55*) and Robinson (*109*) also demonstrated the release of AVP plus neurophysins in humans.

Cryer, et al. (*22*) demonstrated that growth hormones and cortisol are released by smoking and are unaffected by β-blockers. Both are involved in protein and carbohydrate metabolism. Perhaps their effect on plasma glucose helps reinforce the smoking habit. Similar results were found by others (*100, 141, 149*).

Perhaps a factor involved in maintenance of smoking is the increased lipolysis due to release of catecholamines and glucocorticoids. A common reason given for returning to smoking is weight gain (*150*).

Other endocrinological effects of nicotine include increased gastric HCl secretion (*24, 89*), decreased pancreatic bicarbonates and water secretion secondary to inhibition of secretin (*11, 12, 13, 25*), changes in placental hormones (*21, 122*), alteration in prostaglandin formation (*144*), and delayed LH surge in female rats (*85*). Also, it is known that in smokers there is decreased sperm quality and distribution (*117*). Smokers and nonsmokers do not seem to vary in LH, TSH, T4, and FSH (*149*), however.

Cessation of the Smoking Habit

Early Effects of Cessation

Cessation of smoking is associated with alterations in CNS, cardiovascular, and other physiological functions. Whether these are true "withdrawal" phenomena characterized by a rebound or merely a return to normal levels still remains to be determined. It is evident, however, that significant changes do occur.

A number of physiological changes have been observed on withdrawal from tobacco. Decreases in heart rate and diastolic blood pressure are observed as early as 6 hours after withdrawal (*91*). These changes persist for at least 3 days (*71*), (*146*) and perhaps for 30 (*37*). Decreased excretion of both adrenaline and norepinephrine (*92*) and various metabolic changes have also been observed (*37*).

These metabolic and peripheral effects, which are often associated with decreased arousal, have been supported by EEG studies showing increases in low-frequency activity (*135*) and alterations in cortical alpha frequencies (*72*). Ulett and Itil (*135*) recorded cortical EEG from heavy smokers (one pack of cigarettes per day) in an attempt to detect EEG changes associated with acute withdrawal. Baseline EEG measurements were obtained while the smokers engaged in their normal smoking pattern and were compared with data from the same individuals after they were deprived of tobacco for 24 hours. It was found that there was a significant increase in the low-frequency EEG bands (3-5-7 cycles/sec) during deprivation. This effect was readily reversed after the subjects smoked two cigarettes within a 5-minute period.

In a similar study, Knott and Venables (*72*) did a computer analysis of cortical alpha activity in male nonsmokers, smokers asked to abstain for a 13- to 15-hour period, and smokers who continued their normal pattern of smoking. Analysis of variance of pre-smoking alpha activity indicated the mean alpha frequency of the subjects in the deprived group was significantly lower (9.3 Hz) than in the nonsmoking group (10 Hz) and nondeprived group (9.9 Hz). When the deprived group smoked two cigarettes, the alpha frequency increased to the levels of the nonsmoker and smoker control groups. Thus, there is evidence for a rebound effect and a true withdrawal reaction. The data are interpreted as indicating that deprived smokers are in a state of cortical "hypo-excitation," and that smoking has the effect of increasing excitability to levels comparable to those found in nonsmoking and nondeprived groups. Since all groups were equal on measures of extroversion, the authors hypothesize that they have described a true "smoking factor" rather than a difference due to personality. Alternatively, one could conclude from the same data that the results obtained are due to the removal of an arousal-producing drug from a group of people who are ordinarily hypo-aroused.

Numerous other physiological changes have been noted to occur after cessation of smoking. Ejrup (*27*) reports that weight gain is a common sequela to cessation. Although not generally observed, he reported that, in a number of patients, blisters in the mouth occurred along with constipation upon cessation of smoking. If the patients resumed smoking, the blisters disappeared.

Krumholz, et al. (*74*) have measured changes in cardiopulmonary function at rest and during exercise 3 and 6 weeks after cessation of smoking. All subjects had smoked more than one pack of cigarettes a day for at least 5 years. Changes during exercise were measured on the standard bicycle-ergometer test. Following 3 weeks of abstinence, heart rate, oxygen debt, and ratio of oxygen debt to total increase in oxygen uptake during exercise were significantly reduced. In addition, expiratory peak flow and D_l were significantly increased. Pulmonary

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16. BEHAVIORAL FACTORS IN THE ESTABLISHMENT, MAINTENANCE, AND CESSATION OF SMOKING.

that, from the perspective of social learning theory, smoking is seen as a learned behavior from the onset.

The analysis continues as follows: Discriminations between situations in which smoking is punished socially and those in which it is either ignored or favorably received are formed, and various circumstances (both external and internal) begin to control smoking. Insofar as they are associated with smoking, some situations, such as an empty cigarette pack or an annoying telephone call, may serve as conditional stimuli (CS's) which elicit covert responses. These responses (i.e., physiological changes or discomfort, perceived as craving) increase the likelihood of smoking. In turn, they can serve as discriminative stimuli (SD's), setting the occasion for the reinforcement provided by smoking. Moreover, stimuli which are preparatory to the act of smoking, such as the sight of a cigarette, can function as secondary reinforcers for behaviors preceding them (for example, purchasing a full cigarette pack). These cues can also serve as discriminative stimuli for behaviors which follow them, such as lighting the cigarette, thus forming a linked chain of responses (a smoking ritual). For successful termination of the overt act of smoking to occur, the extinction of most or all of the conditional stimuli, secondary reinforcers, and discriminative stimuli which make up the habit is required. The way in which these ideas have been put to specific use in therapy will be discussed in some detail later in this chapter.

The number of emotional events which can influence smoking are potentially quite great. If smoking is seen, in part, as an avoidance/escape response to aversive withdrawal states, then, hypothetically, by a process of stimulus generalization, other dysphoric states (for example, anger, tension, boredom) might also serve as discriminative stimuli for smoking. Also, response generalization may occur. In this case, the smoking ritual serves as a temporary escape (coping response) from various aversive situations (that is, smoking as a response which provides relief). Smoking can be seen, therefore, as a generalized primary and secondary reinforcer providing both positive and negative reinforcement over a remarkably wide array of life situations.

From a social learning theory perspective, smoking is difficult to modify because of its ability to provide immediate reinforcement—nicotine from an inhaled cigarette reaches the brain in seven seconds (twice as fast as intravenous administration from the arm). Furthermore, the habit is tremendously overlearned: at ten puffs per cigarette, the pack-a-day smoker gets more than 70,000 nicotine "shots" in a year—a frequency which is unmatched by any other form of drug taking (*40*). While most smokers recognize that sustained smoking can lead to a variety of unpleasant events, ranging from bronchitis to lung cancer, the ultimate aversive consequences of smoking—though potentially of great magnitude—are delayed and therefore have less

influence over ongoing smoking behavior than immediate consequences. This is a situation common to a number of self-management problems (*37*). Unlike alcohol and many other drugs of dependence, there are few immediately noticeable negative consequences (*40*).

To a large extent, behavioral researchers have *assumed* relationships between environmental events and smoking. Treatment practices have been based on general theory rather than on research or a functional analysis of smoking behavior as such. Thus, though part of the promise of social learning theory has been fulfilled, and behavioral concepts may have generated new standards of effectiveness in the treatment of smoking, there has not been a comparable contribution to the understanding of smoking per se.

The Nicotine Addiction Model

A physiologically based model of smoking, emphasizing the key role of nicotine as a reinforcer, has evolved from the work of Schachter (*42, 43*) and others like Jarvik (*19*) and Russell (*40*). The main focus is on explaining the maintenance of the smoking habit following acquisition. Under this formulation, smoking is viewed as an escape/avoidance response to aversive stimulation provided by periodic nicotine withdrawal in the addicted smoker. An internal regulatory mechanism is implied which detects the level of nicotine and maintains it within characteristic upper and lower limits by regulating the frequency of smoking (and possibly other intake parameters).

Much of the evidence in support of smoking as negatively reinforced behavior comes from a series of innovative experiments conducted by Schachter and his associates over a 10-year span. In one study, Nesbitt (*30*) used the amount of shock a subject was willing to tolerate as a behavioral measure of anxiety. They found that heavy smokers tolerated a higher shock intensity (were less "anxious") when allowed to smoke than when not allowed to smoke; nonsmokers tolerated an intermediate shock intensity. The design did not allow a differentiation between the possibility that smokers tolerated higher shock intensity because of a "sedative" effect of smoking (positive reinforcement) or because smoking constituted escape from withdrawal symptoms perceived as "anxiety" (negative reinforcement). To test for this, Silverstein (*46*) varied the amount of nicotine in cigarettes given prior to shock presentation. He found that smokers given a high-nicotine cigarette tolerated more shock than smokers given low-nicotine cigarettes and that there was no significant difference between smokers given low-nicotine cigarettes and deprived smokers. He concluded that the sensory-motor and oral positive reinforcement provided by low-nicotine cigarettes played a negligible role in increasing shock tolerance compared with the negative reinforcement provided by escape from withdrawal symptoms using high-nicotine

cigarettes. Further support came from the observation that nonsmokers exhibited higher endurance thresholds (lower "anxiety") than deprived or low-nicotine smokers. This suggests that "smoking doesn't reduce anxiety or calm the nerves [but rather that] not smoking increases anxiety by throwing the smoker into withdrawal" (*54*). Thus, a nicotine deficit seems to exacerbate the distress induced by aversive shock. Heimstra, et al. (*15*) found the same effect for psychomotor performance on a simulated driving test.

The next problem was to account for why smokers smoke more when stressed. According to Schachter (*42*), the debilitating effects of no or low nicotine are the result of withdrawal, and the effect of stress is to put the smoker into withdrawal by depleting the available supply of nicotine. This hypothesis was strengthened and new leads were generated by biochemical studies showing that, while some nicotine is catabolized (mainly in the liver, at a constant rate determined in part by the duration of the habit), a fraction of the nicotine escapes detoxification and is eliminated directly in the urine. Furthermore, the rate of urinary excretion is rapid, increases linearly with dosage, and increases as the pH of the urine becomes more acid. The hypothesis was confirmed by direct manipulation of urinary acidity through the administration of mild acidifying agents like ascorbic acid or glutamic acid hydrochloride or alkalizers like sodium bicarbonate (*43*). In addition, stressful events associated with heavier smoking increased urinary acidity and nicotine excretion in the expected direction (*42*). To test whether stress or urinary pH or both were the independent variable, Schachter et al. (*43*) independently manipulated stress and pH and reported that smoking seemed to be under the control of urinary acidity rather than stress as such.

Schachter's model posits that nicotine is the primary reinforcer because of its role in reducing tension and distress associated with nicotine deprivation. If this is true, secondary reinforcers should be relatively unimportant. For example, smokers should not smoke nicotine-free cigarettes, and supplying alternative sources of nicotine should eliminate the desire to smoke. According to Jarvik (*19*), much of the evidence for the role of nicotine as the primary reinforcer in cigarette smoke is circumstantial. Smokers evidently prefer cigarettes with, rather than without, nicotine; but they will smoke nicotine-free cigarettes for a while if no others are available. The fact that smoking such cigarettes is not sustained despite the usual cues for smoking suggests that the other variables are secondary reinforcers that extinguish when nicotine—the primary reinforcer—is not present. Attempts to investigate the role of nicotine as the sufficient condition for smoking, however, have produced conflicting results. Preloading nicotine, by having subjects smoke or chew gum containing nicotine before testing, did reduce subsequent puffing (*20, 21, 25*). And administration of the drug mecamylamine, which functioned as a nicotine "antagonist," increased the smoking rate (*52*). But Kumar, et al. (*21*) were unable to demonstrate a dose-response effect on subsequent smoking when nicotine preloading was administered intravenously. The fact that lettuce cigarettes reinforced with nicotine were as unacceptable as non-nicotine cigarettes also seems to undermine the nicotine-only hypothesis (*19*). Jarvik (*19*) concluded that nicotine may be a *necessary but not sufficient* condition for smoking behavior to occur and to be sustained and that more research is clearly needed to settle the issue of whether nicotine functions as the primary reinforcer or as a "reinforcing co-factor."

The nicotine addiction model suggests that the smoker regulates nicotine levels under widely varying conditions. It implies a mechanism which senses nicotine and provides the impetus for directed behavior—possibly a central "nicostat" or the integration of the various peripheral drug effects of nicotine. While the model is plausible and straightforward, critical tests have yet to be performed. Particularly, direct measurements of changes in nicotine titer and of the withdrawal state have not been attempted. Finally, among variables not adequately explained by the model are the role of environmental stimuli in the control of the habit, the nature of individual differences in smoking behavior (for example, light versus heavy smokers and occasional versus chronic smokers), and the mechanism(s) by which relapse occurs following withdrawal (*35*).

A Context for Behavioral Research on Smoking

Clearly, neither social learning theory nor the nicotine addiction model alone can provide a complete understanding of smoking at present. A recent model, the opponent process theory (*47, 48, 49, 53*) does attempt to link psychological and physiological factors involved in the maintenance of smoking in a more comprehensive fashion. The principal features of the opponent process model as it applies to smoking are as follows: (*1*) the reaction to cigarette smoke is biphasic, with a brief pleasurable component (*a* process) followed by a more sustained dysphoric component (*b* process); (*2*) the hedonic tone—pleasurable A state or dysphoric B state—is determined by the algebraic sum of the two opponent processes at a given point in time; and (*3*) stimuli associated with a given state can elicit this state as a conditioned response after repeated pairings.

The opponent process model assumes that cigarettes contain substances which provide pleasure (initiate the *a* process) during early use. While there may be some unpleasant effects on the first few occasions, these should be offset by the drug effect or by other reinforcers such as peer pressure; if not, the act of smoking will not continue. As cigarette smoking becomes established, the opponent

The remainder of the present discussion will re-examine some of the phenomena of acquisition, perpetuation, and termination of smoking from the point of view of the three models. Special attention will be given to implications for further research.

The Establishment of Smoking

The establishment of smoking can be seen as the result of initial experimentation with cigarettes repeated sufficiently often for acquisition of a habit and/or for addictive processes to take hold. Among the major variables contributing to initiation are social pressure and imitation of peers or family members who smoke (*1, 11*). The following variables influence the decision to smoke: peer pressure, best friends who are smokers, parents who smoke, adolescent rebellion, imitation of adult behavior, and misconceptions concerning the risks of smoking. A recommendation to conduct longitudinal comprehensive studies on the acquisition of smoking in the natural environment, and to determine the conditions under which smoking does or does not begin, would seem especially appropriate.

Once the smoking habit is acquired, the stage is set for addictive processes to contribute to the maintenance of the habit and to its overdetermination under the influence of the variables alluded to in the several smoking models. Additional physiological variables and explanatory variables from personality theory and typology studies (both types described elsewhere in the present report) are clearly relevant. These two sets of variables suggest a number of possible mechanisms by which acquisition might take place, although, as Leventhal and Cleary (*22*) point out, they are not necessarily the same mechanisms which contribute to onset. The need for careful, directed research in this area is evident to achieve a better understanding of onset and acquisition which may lead to more effective methods for prevention and treatment.

A promising approach to the investigation of physiological and behavioral, as well as psychosocial, factors in acquisition comes from animal research. Some studies have shown that nicotine facilitates conditioned-avoidance behavior as well as positively reinforced behavior in rats (*51*) and that it reduces social or pain-induced aggression in both animals and humans (*18*). Analogues of addiction might also be explored in the laboratory. While the laboratory approach might seem artificial to some, increasing experimental control by restricting extraneous variables has been useful in other difficult areas, such as alcoholism (e.g., Nathan and O'Brien (*29*)) and heroin addiction (e.g., O'Brien, et al. (*32*)). If such explorations are successful, subsequent research could be conducted under increasingly complex and more "natural" conditions. Finally, studies of different methods for deterring smoking in children (e.g., Evans (*7*) and Piper (*34*)) should

increase understanding of the conditions under which smoking begins and allow us to identify those environmental patterns which facilitate the movement from "experimental" smoking to addiction.

The Maintenance of Smoking

Once smoking is established as a habit, a number of factors contribute to its persistence and resistance to change. Each of the formulations described above devotes considerable attention to the phenomenon of maintenance, and a large body of research has been carried out from various points of view. In a sense, maintenance can be seen as a stage of smoking characterized by steady-state behavior. Pattern consistency is provided by environmental influences through stimulus control as well as by underlying physiological processes regulating consumption within characteristic limits. As an acquired motivation, smoking constitutes a behavioral pattern with powerful reinforcing value, overdetermined to a remarkable degree by its generating mechanisms. A better understanding of these processes is needed.

With a few exceptions, the determination of environmental influences on smoking has received relatively little direct attention experimentally, despite the fact that treatment techniques based on social learning theory have been used extensively. Among the better examples of a functional analysis of behavior is a study by Griffiths, et al. (*12*). Following detoxification, alcoholics in a residential laboratory were allowed to consume ethanol at certain times, and the amount of tobacco smoked was measured under various conditions. Cigarette smoking was shown to increase from 26 to 117 percent when the solutions consumed contained ethanol. The effect was robust, was observed in each of the five subjects, and was replicated 15 times employing a within-subject design. Control procedures indicated that the effect did not depend on: (1) the pattern of ethanol ingestion, (2) adjunctive maintenance through social interactions, (3) the pattern of days in which the ethanol or ethanol-free vehicle was scheduled, (4) alterations in the portion of cigarette smoked or the number of puffs taken, or (5) knowledge that a given drink did or did not contain ethanol. The study constitutes a good demonstration of the potential of the experimental analysis of smoking behavior, and the method should be extended to other problems of interest.

Smoking as an avoidance/escape response to withdrawal implies an internal regulatory mechanism by which the levels of nicotine (or other substances) are maintained within limits characteristic for each smoker. To get at these processes in research, measures should be taken of smoking behavior (specifying variables such as puff frequency and duration, depth of inhalation, amount of nicotine drawn from a standard cigarette), of major physiological variables (for example, cardiovascular changes, relevant biochemical activity including cholin-

Mr. BLILEY. Let me illustrate. Number one, a supposed revelation concerns the tar and nicotine levels in cigarettes and how they have been affected by what some have called secret processes employed by cigarette manufacturers.

Your testimony refers to this as manipulation, as others on this subcommittee and in the media have done, claiming that, had you known about companies' ability to manipulate the amount of nicotine in cigarettes, you would have regulated them.

Mr. Califano, your 1979 Surgeon General's report devoted numerous pages discussing the decline in tar and nicotine levels, and in the preface on page 12 you noted that this decline resulted from important changes in cigarette production technology, the development of tobacco sheet reconstitution, improvements in cigarette filtration and cigarette paper, the generic manipulation of tobacco strains, and increased use of plant stems and other tobacco portions formerly regarded as waste.

Two, your testimony today also notes that had the Government been privy to companies' information about the addictive nature of cigarettes, the 1979 Surgeon General's report would have found them addictive and would have moved to regulate them. But despite the 1979 report's equivocation on the issue of addiction as compared to the successor 1988 report, nicotine and smoking is referred to as an addiction in a number of places.

For example, in the preface on page 15, your Surgeon General report stated, and I quote, "Yet perhaps because nicotine is a powerful addictive drug, millions of smokers seem unable to translate this information into personal action."

On page 11, your Surgeon General report stated other studies suggest that very few smokers can satisfy their addiction on less than 10 to 12 cigarettes daily. And on page 97 of chapter 14 your report noted that nicotine has long been viewed by some persons as an addictive drug.

You then quoted the following statement from the third report of the Royal College of Physicians of London, 1977, and I quote, "Tobacco smoking is a form of drug dependence, different but no less strong than that in other drugs of addiction."

Three. Let's talk about some of the supposedly suppressed cigarette company research that, had you been privy to while at HEW, you would have acted differently. Despite what may be said in the press, this subcommittee so far has only heard in detail from the research of a former cigarette company employee, Dr. Victor DeNoble. So I have to assume that his work is included in your charge. However, Dr. DeNoble made clear at our last hearing that his work did not prove addiction. He simply found that rats would self-administer nicotine and thus that it was a positive reinforcer. Let me quote from page 11 of chapter 15 of the 1979 Surgeon General's report: "Research has shown that animals may self-administer nicotine."

On page 7 of chapter 16 your report referred to several works that "emphasize the key role of nicotine as a reinforcer."

On page 7 of chapter 15 the 1979 report stated, "Whether or not nicotine is the only reinforcing agent, it is still the most powerful pharmacological agent in cigarette smoke." Nicotine's role as a primary reinforcer is referred to throughout the report.

So let me sum up. Mr. Califano, you come here today to claim that the cigarette companies conducted a disinformation and suppression campaign regarding the issues that you note have been in the press and considered by this subcommittee recently: So-called nicotine manipulation by secret processes employed by cigarette companies, the decline in tar and nicotine levels of cigarettes and what that means in terms of receipt by the smoker, animal tests that demonstrate that animals will self-administer nicotine, the role of nicotine in cigarettes as a positive reinforcer, and the debate over the addictive nature of nicotine in smoking.

You claim that, equipped with this supposedly suppressed information, you would have acted differently during your tenure at HEW. Yet a report that you authored 15 years ago raises all these same issues, makes these same findings, or refers to sources that did. This proves that you did have the information that some would have us believe has only recently emerged and again that nothing is new here. Isn't that correct?

Mr. CALIFANO. Mr. Bliley, it is not correct. If I may respond, there was an enormous debate at HEW when I was Secretary on the issue of whether or not cigarettes were addictive, and the articles that you are citing, they were articles on the other side of those issues in that same Surgeon General's report that were attached as part of the accumulation of data.

I personally, as I indicated in my testimony, tried to get Surgeon General Richmond to formally declare cigarettes addictive and nicotine addictive as Surgeon General Koop was able to do 10 years later. I was—I recognized the dangers of smoking, and I wanted to alert our people to them.

The medical evidence, the research was not there. Had we had the additional research of the tobacco companies—and I hope the tobacco companies will come forward with every single bit of research and every document they have in this area so that we can lay all this out—we would have moved much more aggressively. We would have welcomed the opportunity to regulate cigarettes.

Second, it is the relationship between addiction and manipulation that makes the manipulation so sinister. The tar was coming down, cigarettes—they were producing low-tar cigarettes and low-nicotine cigarettes—in quotes—trying to deceive the American people in saying, "These are healthier cigarettes; you can smoke these."

Well, we now know—we now know that was nonsense, they are not healthier cigarettes, they create cancer, they create heart disease, they create emphysema. So we did not have the formal finding, and C. Everett Koop, who was as aggressive as any Surgeon General in the history of this country in battling cigarettes, was unable to make that finding until he had been in office a while.

Mr. BLILEY. But you admit—in your statement you said that there is no such thing as a safe cigarette.

Mr. CALIFANO. That is correct.

Mr. BLILEY. And so you had the information.

Thank you, Mr. Chairman.

Mr. WAXMAN. Thank you, Mr. Bliley.

Mr. Wyden.

Mr. WYDEN. Thank you, Mr. Chairman, and thank you for an excellent presentation, Mr. Califano.

Let me join Chairman Waxman in saying that I also am very glad that you are speaking out about the tobacco industry's attempt to silence you. In my view, you are doing what the tobacco industry fears most, and that is speaking out, bringing the scientific facts to the American people, letting our citizens see the health consequences of smoking, and my view is we are going to win this fight because people like yourself, people in positions of influence, are willing to come forward, take risks, and we commend you for it.

Mr. CALIFANO. Thank you, Mr. Wyden.

Mr. WYDEN. Let me, if I might, start by asking you this. As a former attorney, I wonder if you might comment further on news reports alleging that tobacco industry lawyers sought to insulate tobacco companies from liability. My question to you is, what would have been the ethical course for tobacco company attorneys who allegedly had access to research and studies indicating severe health impacts relating to smoking?

Mr. CALIFANO. I think there are a whole series of ethical issues. I think these are not easy questions, Mr. Wyden, for lawyers to face. I do think that the legal profession in this area has got to take a hard look at itself, that when you begin to say either destroy documents—and I don't know whether anyone said destroy documents here, but we will see over time, I am sure—when you begin to say don't conduct research, when you begin to say move the research out of the United States so it can't be subpoenaed, we don't want anyone to find out that we have this evidence that cigarettes kill or that cigarettes cause heart disease when we are being sued by people, I think there are serious questions about the ethics.

There are ethical questions across the board here. I mean, what of the ethics of scientists keeping—keeping this secret? What of the ethics of businessmen who maintain their profits by selling something, saying things about it they know not to be true, suppressing the evidence that they are lying as they are selling their product? There are really serious ethical questions throughout.

I mentioned the legal profession because I spent so much time as a lawyer, and I think there really are profound issues here that I hope the American Bar Association, Bill Hide, the president, will take a good look at.

Mr. WYDEN. Let me ask you a question about Medicare, and again I think this is an exceptional contribution you are making.

I remember all my days in senior citizens centers, and you virtually walk in and you see the horrible consequences of smoking with seniors and others suffering, and I think it is a great contribution you are making with this Medicare analysis, and I am very troubled by something I saw in one of the papers this morning indicating that you felt that the share of Medicare costs attributable to tobacco was going to increase because women who are heavy smokers—this was reported in the New York Times—are beginning to enter the covered 65 and older group.

I have seen some trends along the lines of what you said with advertising that would suggest that this is going to be a very serious problem, because a lot of the tobacco company advertising real-

ly seems to target young women, and so what you have is a situation where young women get addicted very early on, and then I gather there is a prospect based on your report that this is a significant factor in raising Medicare costs. Could you comment on that aspect?

Mr. CALIFANO. I think it is a significant factor. We have to remember that the heavy smoking by women came almost a generation after the heavy smoking by men, and women who smoked a lot are just beginning to enter the over-65 group, and that will undoubtedly have the impact of increasing costs on Medicare.

There is an element here that really is truly disturbing. I noticed in one of the news reports that the tobacco companies had evidence of the ability, potential, I guess, of nicotine to suppress appetite, and one of the things we didn't realize in 1978 was how relevant being thin and continuing to smoke for a woman was because she thought it would help her keep thin, suppress her appetite or what-have-you.

What the cigarette companies bought, what they really bought by this campaign of suppression and disinformation, was the ability to hook millions of American women over that 30-year period because in the beginning of this period they were not smoking at the rates they are smoking at now.

Mr. WYDEN. I think that is a very important point, and my concern is that pattern of trying to target young women is continuing today. What you are talking about is evidence that it took place years ago, and my concern is, you look at the advertisements today and how it seems to be the key to independence for young women and the like seems to reflect a continuing pattern.

Mr. CALIFANO. I would hope, Mr. Wyden, that the committee would give some consideration to looking at the marketing practices of the cigarette industry in this and other areas.

Mr. WYDEN. Let me ask you about the research—and I gather over the last few years this research has accelerated—indicating that when senior citizens who have smoked for a considerable period of time, even in that kind of situation, when they stop, their health can still improve significantly and that there is a prospect for reduced Medicare expenditures. Is that correct, and what is the state of that research?

Mr. CALIFANO. Yes, I think that is. There is research to that effect. I think the Department of Health and Human Services has a lot of it.

I think we have to recognize that what we are talking about is keeping people healthy and independent for a longer period of their life. That will both make the quality of their life much better and reduce the cost to the Medicare program, so that if senior citizens, if older Americans, if middle-aged Americans will quit smoking, they are likely to have much longer periods of independent living and quality living and longer periods in which they won't be a drain on the Medicare trust fund.

Mr. WYDEN. You are absolutely right about this matter of prevention. You know, the Medicare program really shows the insanity of our priorities. Medicare Part A pays these huge checks for hospital bills, the check goes from the Government, you know, to the insurance company, then Medicare Part B pays virtually nothing

for prevention. You know, Medicare Part B has a tiny preventive component.

So I am very hopeful that we can get your message to the Congress about the need to rebuild this system and focus more on keeping people well rather than sick care, and substance abuse is at the heart of it, and we thank you for the contribution.

Mr. CALIFANO. Thank you, Mr. Wyden.

Mr. WAXMAN. Thank you Mr. Wyden.

Mr. McMillan.

Mr. MCMILLAN. Thank you, Mr. Chairman.

I really do hope we can get down to facts so that senior citizens or young people can have sensible guidelines that they can live by and not simply hyperbole.

You mentioned—and I want to try to get a little better understanding of this—that you had received a letter. You didn't state who the letter was from.

Mr. CALIFANO. I did read it. The letter is from a lawyer, apparently a lawyer at King and Spalding.

Mr. MCMILLAN. Is there a signature on it?

Mr. CALIFANO. Yes. It says Theodore M. Hester. It says, "King and Spalding represents Brown and Williamson Tobacco Corporation. We understand that you will participate tomorrow in a hearing of the House Subcommittee on Health"——

Mr. MCMILLAN. I understand. Who is the letter from?

Mr. CALIFANO. Theodore M. Hester, who enclosed a copy of this injunction. It was obviously——

Mr. MCMILLAN. And the letter makes reference to documents. What documents?

Mr. CALIFANO. Let me just read the letter and then——

Mr. MCMILLAN. You don't need to read the letter.

Mr. CALIFANO. It says it may include a discussion of one or more articles appearing recently in the New York Times.

Mr. MCMILLAN. What are those articles?

Mr. CALIFANO. These articles included references to documents believed to have been stolen and which are subject to a State court injunction——

Mr. MCMILLAN. Are they stolen?

Mr. CALIFANO. "A copy of that injunction is being provided to you with this letter."

I have no idea, Mr. McMillan——

Mr. MCMILLAN. Are they stolen documents, Mr. Califano?

Mr. CALIFANO. I have no idea, Mr. McMillan, but the order they enclose purports to prohibit any discussion of these by all persons who are informed of this restraining order, which is, I think—I haven't practiced law in a long time, but I think that is a—certainly unconstitutional.

Mr. MCMILLAN. What is the restraining order that you are referring to?

Mr. CALIFANO. This is a restraining order issued by a judge in Jefferson County, Ky.

Mr. MCMILLAN. What does the order state?

Mr. CALIFANO. Well, let me read it because it is the order by which I think they hope to intimidate me and stop me from testifying.

Mr. MCMILLAN. Is this a Federal judge seeking to intimidate you?

Mr. CALIFANO. It is the hired lawyers for the tobacco company and the tobacco company——

Mr. MCMILLAN. All lawyers are hired as far as I am concerned. But is this a court order?

Mr. CALIFANO. This is a court order signed by a judge named Thomas B. Wine dated January 7, 1994. I don't know if we have any other copies of it, but we may have.

Mr. WAXMAN. Mr. McMillan, would you yield to me?

Mr. MCMILLAN. I would like the Secretary to answer my question.

Mr. CALIFANO. It is an order dated January 7, 1994, signed by Thomas B. Wine, and the order prohibits, as I said, among other things, "All persons who are informed of this are hereby restrained and enjoined from disclosing to anyone other than plaintiffs or intervening plaintiff"—which was Brown and Williamson—"any material or information in the possession of said defendant"—somebody named Williams—"including without limitation, and whether in a category of privilege or confidential or otherwise, all documents, computer discs and drives and other storage retrieval systems and other tangible and electronic materials and things belonging to plaintiffs or any of their clients, including without limitation Brown and Williamson, all information contained therein and thereon, all documents, manuscripts, narratives, reproductions, or using for any purpose in any manner the"——

Mr. MCMILLAN. Please don't read—don't read the letter. I think we are referring to documents that allegedly have been taken, stolen, and are subject to court order with respect to their restitution, and what you are referring to as intimidation is actually the result of an order of a Federal district court judge. Is that correct?

Mr. CALIFANO. This is not a Federal district court judge, this is a judge in—in, as I said, in Jefferson County, Ky.

Mr. MCMILLAN. OK. I stand corrected. It is a State judge.

Mr. CALIFANO. Let me say, you know, I am a lawyer, I have represented a lot of people, I have also been on and off in public life. I have never, ever received anything like this in my life. I am appalled that somebody would send something like this, have it delivered, it arrives on my desk at 5:00 the night before I am supposed to testify here. It is an obvious attempt to say, "We want to intimidate you, we don't want you testifying. Look at this order. We may file something against you. We may try and use up your resources. We"——

Mr. MCMILLAN. I am not a lawyer, I am just a poor lay Member of Congress, but I think it refers to documents that are the subject of court order.

Mr. CALIFANO. It refers to articles in the New York Times. I mean if we can't discuss articles in the New York Times in this country and before this committee——

Mr. MCMILLAN. I do it every day. I don't necessarily accept what they say or what anyone else says, I try to use my own judgment.

But I think the documents are subject to a court order, and I think it is misleading to simply suggest that it was done to intimidate you. That is very much at issue here, as I understand it. I

haven't seen the documents, and I don't know that anybody on the committee have seen the documents.

Have you seen the documents, Mr. Chairman?

Mr. WAXMAN. If you will yield to me, I would like to know if Mr. Califano has these documents.

Mr. CALIFANO. I do not have these documents.

Mr. WAXMAN. So you are being told to not talk about some documents you don't have by some court in Kentucky, and you get a letter from a lawyer saying don't talk about anything that has to do with anything that has to do with these documents, which means even though you have read it in the New York Times, you are not allowed to talk about it. Isn't that what is really going on?

Mr. CALIFANO. Also, in terms of intimidating, we are a small, not-for-profit research, and we do demonstrations for drugs to try and find out ways to help young kids stay off of drugs. We do research. We are about to try a research program for prisoners. We are a very small not-for-profit operation affiliated with Columbia University, and when that kind of a letter and that kind of an order comes, I can't tell you how that shook up people at the Center on Addiction and Substance Abuse. These are young researchers. These are people who have devoted their life to fighting substance abuse, to trying to find out how to help this country fight it, and then some heavy lawyer—heavy law firm comes in and says, "By God, you can't testify, and if you do, we are going to go after your organization or you." That is what this says.

Mr. MCMILLAN. I will reclaim my time. You brought up this issue, I didn't bring it up. I haven't seen the documents. You seem to think these documents contain information that, had you had it some years ago, you would have acted differently, and I think that is a question that we need to raise questions about.

The gentleman from Virginia has very appropriately brought up information that you had access to a long time ago that perhaps would have enabled you to take action or your administration to take an action that it didn't take. So I think what is in those documents may be of interest to us or what is in any other documents that may have been available to the public or to the Secretary of HEW at various—or the Surgeon Generals at various points in time.

Are we on the 5-minute rule today?

Mr. WAXMAN. We are taking turn turns of equal time. It has been over 5 minutes. Do you want to take another minute?

Mr. MCMILLAN. Well, I will see what I can do.

I haven't had a chance. I would really like to be able to get into your study more in more detail, but it was marked for release, I think, today at 10 a.m. Apparently some people got it yesterday. Apparently the press got it before 10 a.m. this morning, and it makes a number of assertions in there that I think really should be examined fully in terms of their import. It is important to determine to what degree substances contribute to death. But I think it is very important that we do that with sufficient detail so that we can really tell the difference.

As I understand it, a very high proportion of causes of death are attributed to substance abuse, and—what is the reciprocal of that? What is it normal to die of?

Mr. CALIFANO. Well, the issue is—there are two issues. One is the issue of disease and what those diseases cost. That is what lays the tremendous burden on the Medicare program, not the deaths, it is the taking care of somebody with emphysema, it is the taking care of somebody with lung cancer, it is the taking care of somebody with cardiovascular disease or chronic bronchitis, and it is the disability that often goes along with that.

These costs, for example, do not include the cost of disability. The Social Security disability system pays, I am sure, at least $2 billion a year as a result of people disabled by smoking. This study—it is the diseases that are the most relevant factor in terms of the cost of the Medicare.

We do lay out as clearly as we know how the exact methodology we do to do this as part of our study, and your staff can examine it. We would be happy to answer any questions. As I said, there is a bibliography of the articles used, but it wasn't based solely on the epidemiological medical information, it was also based on an examination of the hospital records of inpatient Medicare patients.

I also maybe could take this opportunity—I noted that Mr. Bliley mentioned that we indicated in our methodology that we found the elderly population not the focus of medical or epidemiological research; in lieu of elderly-specific relative risks, we use relative risks for the general population.

The fact is that is one of the reasons why these numbers are probably conservative, because the risks for the elderly who have accumulated much—many more years of disability and disease from smoking are more—are likely to be a more expensive population.

Mr. MCMILLAN. When we have had a chance to really study your report, would you be willing to come back and testify on the substance within it instead of the conclusions?

Mr. CALIFANO. I would be happy to testify on any aspect of this report or help this committee and you, Mr. McMillan, any way we can, to provide any information you would like.

Mr. WAXMAN. Thank you, Mr. McMillan.

Mr. MCMILLAN. Thank you.

Mr. WAXMAN. Mr. Califano, we heard from researchers who, in the early 1980's, were doing work on addiction. They had been told by Philip Morris that they, because of a contract with Philip Morris, couldn't disclose their research. They had a confidentiality provision in their agreement as employees of Philip Morris. Now they were able to come before us because we asked the executive from Philip Morris to release them from that confidentiality agreement, and we got some testimony.

Now that is, those confidentiality agreements, are one of the other ways tobacco companies use to try to keep information that they had in-house about tobacco. We have heard about a court order on some documents which evidently a judge in Kentucky feels shouldn't be revealed, but you don't have those documents, do you?

Mr. CALIFANO. Mr. Chairman, I have no documents. I have never seen any documents. I never heard of this judge or this order really, and I also—all I know is, as I can say, is what I read in the newspapers, in the New York Times or the Washington Post.

Mr. WAXMAN. So you are discussing documents based on an article you read in the New York Times.

Mr. CALIFANO. I am discussing documents based on the New York Times articles by Mr. Hiltz.

Mr. WAXMAN. So if a court order would apply to you, as this letter seems to suggest, because you read an article in the New York Times, everyone watching this hearing on C-Span would probably also be enjoined from discussing this information about some documents that had been referred to and characterized in an article that you have talked about from the New York Times.

Mr. CALIFANO. That is right, Mr. Chairman. I think you should note, when people do something like this, it is not only an attempt to intimidate me but it is an attempt to send a signal to anyone else this committee might want to call as a witness to say, "If you are going to go before that committee, you better beware." I mean that is what I mean when I say I also think this is a blatant attempt to obstruct the work of this committee.

Mr. WAXMAN. Well, it is called stonewalling. It is called intimidation. It is trying to put a chilling effect on everybody who might have some information or some ideas about the problems of tobacco and its use and the consequences of it to this country.

You were there in the early days when our policy was formulated 30 years ago in the White House with President Johnson. You were there as Secretary of HEW under President Carter. You indicated that you were very cautious in your decisions as to what you would characterize. You said in your testimony the head of the National Institute of Drug Abuse of the United States said to you as the Secretary that you ought to talk about the addiction from cigarettes; you felt you didn't want to make that statement so unequivocally because you wanted to be absolutely sure of any scientific assertion that was made in any Government position.

I find it amazing to have you criticized now for having known 15 years ago what the executives of the tobacco industry 3 weeks ago still denied, and that was that cigarettes are addictive, and then to criticize you for not having acted on the information because you tried to be responsible and prudent by the way you handled that very issue.

I must say that I am just really quite astounded at the overreaching of the tobacco industry to try to, even at this day, to keep information from getting to the public.

Now you were there when the policy was formulated. Now ironically enough, you are in a position where we are evaluating 30 years of this policy where we did not take further action to stop smoking in this country, and the Medicare program may go broke, health care reform may be a sham, if we have to pay for the enormous health care costs because of cigarette smoking and because people weren't warned about addiction when they decided to experiment, usually as kids, with this particular product. Isn't that really what we are talking about?

Mr. CALIFANO. That is, Mr. Chairman, you are absolutely right, and you put your finger on the most important hot button currently, which is that health care reform is doomed to fail unless we deal with cigarette smoking and, I might add, some of the other

substance abuse too, alcohol and drugs, but cigarette smoking is the number one cost culprit, there is no question about it.

Mr. WAXMAN. Well, I think that is why we have got to stay, on this subcommittee, focused on this issue and not in any way be distracted from our responsibility by ludicrous suggestions that reading articles in the newspaper might well be something that we shouldn't talk about in a very distorted kind of legal reasoning.

Mr. Wyden.

Mr. WYDEN. Just one last question again in terms of the trends you might see in the tobacco industry, Mr. Califano.

There have been a number of stories in the press, most recently again this weekend in the New York Times, about the tobacco industry's very aggressive efforts to promote these markets overseas, particularly in Asia. I think that there was one report, it might have been this weekend or another, that talked about millions and millions of children, for example, in China, in effect, being targets of this kind of smoking campaign.

I wonder if what we are seeing here now is another part of this historical pattern of the tobacco industry to buy time to cultivate another market. It seems to me what you saw again yesterday is try to silence everybody possible. The tobacco industry wants to run the best censorship program that they can, and then buy themselves some additional time in order to get at these very lucrative overseas markets, particularly in Asia.

Is that a view that concerns you? Is that, again, part of this pattern of, they are always trying to look at upcoming markets?

Mr. CALIFANO. Mr. Wyden, I am profoundly concerned about that, not only because of what it says about these individuals, the tobacco companies, in selling their products overseas, often without any of the warnings that we have here, taking advantage of illiterate populations, taking advantage of poor people, and getting them hooked on this drug, but I fear for what damage these companies will do to the country I love, the United States of America, because I was at an international conference in London this February, and there were people from Malaysia, and Columbia, and other parts of the Far East, and in the course of the conference, this colonel, the number two military officer in Columbia, turned to a couple of the Americans, and he said, "We are stopping the export of cocaine from our country. People are dying to stop cocaine from going into the United States. You are pouring cigarettes into our country. You are killing far more of our people and maiming far more of our people than we ever had with this. What are you going to do about it?" And I must say, as an American, I was embarrassed, as were the other Americans that were at that conference.

Mr. WYDEN. As you know, communications, you know, are global, and people in Asia are going to be getting the same facts as we Americans are getting, so the truth is going to get out. I mean I guess the tobacco companies can keep running, but they are never going to be able to hide completely, and I just hope that we can help discourage smoking among young people in our country and also keep the tobacco companies from buying time to addict millions of other youngsters overseas and giving our country a bad name in the process.

Again, thank you for an excellent job in your service.

Mr. WAXMAN. Thank you, Mr. Wyden.

That figure from the New York Times, 50 million people in China will die from our export of cigarettes, I just think that is an incredible statistic.

Mr. CALIFANO. What are the Chinese going to say to our children when they come to really appreciate that fact and who killed those 50 million people?

Mr. WAXMAN. Mr. Califano, you have our deep gratitude for your appearance today, and I want to commend you on your work and your testimony. Thank you.

Mr. CALIFANO. Thank you, Mr. Chairman.

Mr. WAXMAN. We stand adjourned.

[Whereupon, at 11:33 a.m., the subcommittee was adjourned, to reconvene at the call of the Chair.]

REGULATION OF TOBACCO PRODUCTS

THURSDAY, MAY 26, 1994

HOUSE OF REPRESENTATIVES,
COMMITTEE ON ENERGY AND COMMERCE,
SUBCOMMITTEE ON HEALTH AND THE ENVIRONMENT,
Washington, DC.

The subcommittee met, pursuant to notice, at 10:18 a.m., in room 2123, Rayburn House Office Building, Hon. Henry A. Waxman (chairman) presiding.

Mr. WAXMAN. The meeting of the subcommittee will come to order.

Several weeks ago the subcommittee heard disturbing testimonies from the chief executive officers of the major U.S. tobacco companies. Despite the overwhelming preponderance of scientific knowledge, these executives denied that tobacco is a cause of human disease or death.

These views were not new. In fact, tobacco industry representatives have systematically disputed major health findings on the dangers of tobacco for more than 40 years.

This morning we will hear from the chief executive officer of the tobacco industries' research organization, the Council for Tobacco Research.

The tobacco industry established the Council for Tobacco Research, or CTR, in 1954, in response to emerging research reports and public fears over the relationship between smoking and cancer.

Originally known as the Tobacco Industry Research Council, the Council changed its name to the Council for Tobacco Research in 1964, the year the Surgeon General, Luther Terry, declared smoking a major cause of lung cancer.

When it was established, the Council described itself as an agency for research into questions of tobacco use and health. Its research decisions were to be guided by a distinguished Scientific Advisory Board assuring its grantees complete scientific freedom. But as we will learn this morning, secrecy replaced openness and public relations replaced science.

Today we will begin to peel the cloak of secrecy covering the Council for Tobacco Research. The subcommittee is releasing a Majority staff report today that shows from the very beginning the Council was a public relations ploy, a seemingly independent research body whose real purpose was to promote the idea that smoking is safe.

As the documents reveal, the Council for Tobacco Research was invented not by scientific researchers seeking answers to important health questions, but by public relations experts seeking to calm

public fears. And the Council's primary activity was not the scientific search for truth but rather, an extensive and lavishly financed public relations campaign that was in the words of the tobacco executives, "entirely pro-cigarettes."

Last year, in an article entitled "Smoke and Mirrors", the Wall Street Journal accused the Council of being the longest running misinformation campaign in U.S. business history. Federal District Court Judge Sarokin who reviewed documents in the Council's special project file was quoted as saying: "Despite the industries' promise to engage independent researchers to explore the dangers of cigarette smoking and to publicize their findings, the evidence clearly suggests that the research was not independent, that potentially adverse results were shielded under the caption of special projects, that the attorney-client privilege was intentionally employed to guard against such unwanted disclosure, and that the promise of full disclosure was never meant to be honored and never was."

The documents Judge Sarokin viewed remain a closely guarded secret of the tobacco industry to this day. The charges raised by the Wall Street Journal and Judge Sarokin are serious and go directly to the heart of the tobacco industries' credibility.

Today, the subcommittee will explore the extent of the CTR's scientific independence and the nature of its interest in public health. The subcommittee is committed to lifting the veil of secrecy that has surrounded research programs of the tobacco industry. I hope today's hearing will help us understand what tobacco industry science really means.

Before calling on our witness, I want to recognize members of the subcommittee for opening statements and to call on Mr. Bliley first.

Mr. BLILEY. Mr. Chairman, today we will hear in greater detail about the Council for Tobacco Research, a private nonprofit organization that uses funds from the tobacco industry to support research into questions of tobacco use and health. As with other tobacco-related issues that this subcommittee has considered recently, only one side of this issue has been aired in the press. It is, therefore, critically important that once again our deliberations attempt to separate fact from fiction and that we opt for good policy rather than good headlines.

We must approach today's proceedings with an appreciation of the fact that the Council for Tobacco Research has been in operation for 40 years. We must also appreciate the fact that during recent times some members of the public or the scientific community and even of this body have come to see tobacco as an item not worth studying and that any scientific organization that is not actively trying to drive the tobacco industry out of business and smokers underground must be instead promoting tobacco use.

Hopefully members of the subcommittee will treat our witness fairly today and let him explain as fully as he may need to concerning what is undoubtedly a long and complex history.

To emphasize the one-sidedness of this debate, permit me to focus on the second of the purported basis for the requested investigation. In particular, an article that appeared on the front page of the New York Times on May 7. I refer to Chart 1.

The New York Times story claims that an executive of Brown & Williamson Tobacco concluded as early as 1963 on the basis of the company's own research that cigarette smoking had been shown to cause or contribute to the development of lung cancer, heart disease, and emphysema. The article went on to charge that the company had attempted with some success to hide its conclusions on smoking and health issues from the Federal health authorities, the U.S. Congress, and the American public.

Three weeks later a short editor's note buried at the bottom of page 2 of the New York Times below advertisements for Timberland Shoes, Ethan Allen furniture, and a public auction for Persian rugs and sundry other items acknowledged that the earlier Times story had been erroneous and I refer to Chart 2.

According to the editor's note, the earlier article had incorrectly quoted Brown & Williamson's general counsel as saying that the company's research had shown that cigarettes contribute to certain health problems when in fact the general counsel was simply predicting what the Surgeon General was likely to say in his 1964 report to Congress on cigarettes.

Finally, Mr. Chairman, I must regrettably note my concern over the conduct of this investigation. As you well know, these hearings are quite a departure from our usual legislative hearings where it is clear what the universe of inquiry will be.

In this particular case, we are presented with a hearing that could easily encompass any activity of the Council during its 40-year history. I think everyone would agree that without the documents that the Majority intends to focus on, it is impossible for members and staff to properly prepare. Thus, I thought our agreement to share documents made sense.

Your staff did agree to share the Majority staff report with my staff but only on an embargoed basis. I was disappointed to learn that at 4:30 yesterday afternoon my staff was informed that none of the other documents would be available to them until midnight or 1 o'clock this morning. In my years as the Ranking Member on the Oversight and Investigations Subcommittee, Minority staff were afforded timely and adequate access to those documents that were the subject of the hearing. I thought I had the assurances that this subcommittee's investigation would be conducted in a similarly professional fashion. I regret that I was mistaken.

Thank you, Mr. Chairman.

[The charts referred to follow:]

CHART 1

THE NEW YORK TIMES, SATURDAY, MAY 7, 1994

Tobacco Company Was Silent on Hazards

By PHILIP J. HILTS
Special to The New York Times

WASHINGTON, May 6 — Internal documents from a major tobacco company show that executives struggled with whether to disclose to the Surgeon General what they knew in 1963 about the hazards of cigarettes, at a time when the Surgeon General was preparing a report saying for the first time that cigarettes are a major health hazard.

The executives of the company, the Brown & Williamson Tobacco Corporation, chose to remain silent, to keep their research results secret, to stop work on a safer cigarette and to pursue a legal and public relations strategy of admitting nothing.

In more than 100 documents, letters and cables from the 1960's and 1970's that provide a rare look at the internal discussions among tobacco executives, the officials spoke of the hazards of cigarettes and stated plainly to one another that nicotine is addictive.

In one document, the company's general counsel said Brown & Williamson's research had found that cigarettes caused or predisposed people to lung cancer, contributed to heart disease and might cause emphysema. The statements contradict the tobacco industry's contention over the last three decades that it has not been proved that cigarettes are harmful or that nicotine is addictive.

The question of addiction has taken on importance in recent months after the Food and Drug Administration said for the first time that it would consider regulating cigarettes. To establish control over cigarettes, the F.D.A. said, it must show that nicotine is addictive and that tobacco companies intentionally exercise control over the amount of nicotine in cigarettes to maintain smokers' addiction.

Officials of Brown & Williamson, which makes Kool, Viceroy and other brands, refused to comment on the documents but sent a letter to The New York Times today suggesting that the documents had been "stolen by a former employee of a law firm doing work for Brown & Williamson." The company said the documents should not be disclosed because some of them may be subject to attorney-client privilege and may be covered by an injunction forbidding their release. The injunction was issued by Judge Thomas B. Wine of Jefferson Circuit Court in Louisville, Ky.

Judge Wine is presiding over a case in which Brown & Williamson is suing a man named Merrell Williams, who they say stole documents from the company.

A lawyer for The New York Times Company, Adam Liptak, said he did not believe that the injunction applied to the newspaper. "Under the Supreme Court's decisions, injunctions may be directed only to specific parties to a lawsuit," he said. "Injunctions directed to the whole world are ineffective."

Some documents were obtained by The Times from a Government official who was disturbed about the testimony in the House last month by the top executives of the seven biggest American tobacco companies, in which they said that nicotine was not addictive. The official said that the documents were also given to Representative Ron Wyden, Democrat of Oregon, a smoking opponent who has been working on investigations of tobacco companies in recent weeks. Mr. Wyden said that he had found the documents to be "very disturbing" and that he had turned over the documents to Representative Henry A. Waxman, chairman of the House Energy and Commerce Subcommittee on Health and the Environment.

Mr. Waxman's subcommittee has held several hearings on the tobacco industry, including the one at which the top executives testified. Mr. Wyden asked each of the executives whether in his opinion nicotine was addictive, and each answered no.

Thomas E. Sandefur Jr., the chairman and chief executive of Brown & Williamson, said in his testimony, "I believe nicotine is not addictive." In response to a request for any research the company has on nicotine and addiction, he said he would turn over documents, but added, "We do not have any animal research."

CHART 2

THOMAS J. BLILEY JR.
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Congress of the United States

House of Representatives

Washington, DC 20515-4607

May 24, 1994

Dear Colleague:

The New York Times article filled with inaccuracy was front page news while the correction was in tiny print buried inside the newspaper. As Paul Harvey would say: "And now for the real story"

The New York Times

NEW YORK, SATURDAY, MAY 21, 1994

Editors' Note

A front-page article on May 7 reported that internal documents showed evidence of a debate among tobacco industry executives in 1963 on whether to disclose what they knew about the hazards of cigarettes.

While the documents do provide evidence of such a debate, several paragraphs of the article, including one paragraph on the front page, described part of one official's report incorrectly.

The article quoted the general counsel of the Brown & Williamson Tobacco Corporation, Addison Yeaman, as saying the company's research showed that cigarettes contributed to lung cancer, heart disease and emphysema.

In fact, Mr. Yeaman was not describing Brown & Williamson's own research but was predicting what the Surgeon General would soon say in the first major report on the hazards of smoking.

Page 2

Mr. WAXMAN. Before I call on our next colleague, I want to indicate to Mr. Bliley that the documents that will be referred to today are not documents that Brown & Williamson has argued about. We have shared documents that we received from the tobacco industry as quickly as we have been able to share them with the Minority. The staff report which was produced today was shared in advance with the Minority. We will continue to attempt to be as cooperative as possible with you and your staff so that we can have a full and fair hearing.

Mr. Synar.

Mr. SYNAR. Thank you, Mr. Chairman.

The Council for Tobacco Research has spent the past 3 decades bullying scientists into reporting that cigarettes are less cancer causing than private and government-funded subsidies have found.

The Council for Tobacco Research has refused to publish studies that the tobacco companies did not approve and the CTR has structured itself so that all research results are protected by attorney-client privilege.

The purpose of attorney-client privilege is not to allow attorneys to aid and abet tobacco companies' fraud on the American people. Attorney-client privilege does not protect attorneys who squelch findings of cigarettes causing cancer in rats nor does it protect attorneys who falsely deny the health hazards of smoking to Congress.

We need to be asking ourselves, "Are the attorneys employed by the tobacco companies functioning as counsel or as tobacco company executives?" Does the attorney-client privilege extend to decisions made by the CTR and tobacco company attorneys to fund or not to fund a project or to withhold study results?

I hope we are able to learn more today about the practices of the Council for Tobacco Research, and I look forward to further inquiries into the approaches used by the tobacco industry attorneys in shielding their clients' conduct from public scrutiny for over 30 years.

Thank you, Mr. Chairman.

[The opening statement of Mr. Synar follows:]

STATEMENT OF HON. MIKE SYNAR

Ladies and gentlemen, the subcommittee is holding this hearing to shed some light on the activities of the Council on Tobacco Research (CTR) over the past 40 years. The country's largest cigarette companies set up CTR in 1954 to provide the American people with what was supposed to be objective scientific evidence of the effects of smoking on one's health.

We know today that CTR has spent the past 3 decades bullying scientists into reporting that cigarettes are less cancer-causing than reported by privately- and government-funded studies. We also know that CTR has refused to publish studies that were not to the liking of tobacco companies, and that CTR structured itself so that all research results would be protected by attorney-client privilege. These activities are detailed in the February 11, 1993, Wall Street Journal article that I have attached to this statement. [See p. 97].

Attorney-client privilege is intended to encourage a client to fully disclose his or her activities to an attorney, so that the attorney can provide the client with competent representation. It is not the same as the privilege which exists between a clergyperson and parishioner or a doctor and patient. Those are relationships of conscience or health. An attorney is there to defend a client in court.

The purpose of the attorney-client privilege is not to allow attorneys to aid and abet tobacco companies' fraud upon the American people. Attorney-client privilege does not protect attorneys who squelch CTF's findings of cigarettes causing cancer

in rats; nor does it protect attorneys who falsely deny the health hazards of smoking to Congress.

We need to be asking ourselves, are the attorneys employed by tobacco companies functioning as counsel or as tobacco company executives? Does attorney-client privilege apply to decisions made by CTR or tobacco company attorneys to fund or not to fund a project or to withhold study results?

I hope that we are able to learn more about the practices of CTR today, and I look forward to future inquiries as to the approaches used by tobacco industry attorneys in shielding their clients' conduct from public scrutiny over the past 30 years.

Mr. WAXMAN. Thank you, Mr. Synar.

Mr. McMillan.

Mr. MCMILLAN. Thank you, Mr. Chairman.

First, I would like to thank Dr. James Glenn—I don't think anyone has thanked you yet—for joining us today to discuss the issues related to studies funded by the Center for Tobacco Research. It is my understanding that the center engaged in funding of specific disease-related research and the understanding of it for over 40 years.

Before we get to those matters, I have a few questions which should be asked at the beginning of this hearing.

We have spent a great deal of time on the issue of tobacco and more than a few people, myself included, are interested in finding out what it is we hope to accomplish other than satisfying an addiction to public attention. I was present when we recently voted legislation out of this subcommittee that restricts smoking in public places. Although it took several informational hearings and three markup attempts before we were successful, that legislation is now in the hands of the full committee.

Since that legislation has moved, why are we continuing to hold hearings on tobacco? Does the chairman propose to address specific legislation and, if so, what is it?

Mr. Chairman, if you would grant us the courtesy, it would be nice to evaluate the information which we obtain in the light of some specific proposal. As yet, you have identified no specific legislative goal which these hearings are intended to further. As always, I would be interested to consider your legislation on its merits and on its impact on people instead of repeatedly beating the tobacco industry into the ground without apparent legislative purpose. The members of the subcommittee obviously feel they know enough about the issue generally, otherwise you might have a greater attendance record. Perhaps if you offered a legislative proposal which we could focus upon you would get as many members here as we do TV cameras from time to time.

Mr. Chairman, if we have legislation, let's consider it. If not, let's quit perpetuating classic government—spinning wheels, accomplishing nothing, wasting the time and money of everyone except for lobbyists, lawyers and public relations experts.

There are other issues such as the reauthorization of the Safe Drinking Water Act, or health care reform which we could and should be working on in this subcommittee. As a matter of fact, I am going to leave in 2 minutes to go do just that with respect to trying to shape a health care reform proposal that the Energy and Commerce Committee might find a majority to support.

I would like to conclude with one final query. I received just a few minutes ago a thick sheaf of documents that is labeled "the

Hill and Knowlton documents: How the Tobacco Industry Launched its Disinformation Campaign", which I understand was taken from files in some depository.

Could I ask the question, if these papers include all of the matter that was in those files? Or have they been selected for a specific purpose and other documents concealed?

With that query, I yield back the balance of my time.

Mr. WAXMAN. I think the gentleman has asked a number of questions and made some comments and I ordinarily wouldn't seek to respond, but I feel I must.

I can't think of anything more important for this subcommittee, which is the Health Subcommittee, to do than to inquire about tobacco, which kills over 400,000 Americans each year. For 40 years, we have had a veil of secrecy by the tobacco industry on what they have known, what they have done, and how they have tried to package and convince the American people to disregard the overwhelming scientific information about the dangers from tobacco.

We have been fair in this subcommittee to the chief executive officer of Brown & Williamson when his lawyers called and asked, we gave them a postponement. One would think they would want to come forward and answer all the news articles that have charged them with serious, serious dereliction of responsibility to the public. In fact, actions that would make one believe that they have been engaged in a conspiracy to hide from the American people information that they knew early on about addiction of cigarettes and the dangers from cigarettes which even to this day they did know.

We think that the tobacco industry should be forthcoming and go on the record and inform not just the oversight responsibilities of this committee but for the purposes of developing a record for legislation. We have the bill on environmental tobacco smoke, which this subcommittee has reported. But we have Mr. Synar's bill which would give the FDA jurisdiction over cigarettes, the first time any government agency would have regulatory jurisdiction over tobacco. I have sponsored legislation as well dealing with the advertising of tobacco products.

So I think what we are doing is quite appropriate and the way we intend to proceed and have proceeded is eminently fair and I intend to continue to call the hearings when it is appropriate for the subcommittee and when it will give an opportunity for the tobacco industry to speak on the record and to answer inquiries which they even refuse to this day to answer when asked by responsible press.

I thank the gentleman.

Mr. MCMILLAN. Will the gentleman yield?

Mr. WAXMAN. I certainly will.

Mr. MCMILLAN One of the themes of this hearing today will probably be the fact that we had a group of attorneys in this institute who were making judgments about scientific research and I would submit that the activities of this committee are precisely the same thing. We have a group of lawyers who are trying to make judgments about scientific research.

What I would like to do is to examine the fact with respect to the two pieces of legislation that you mentioned and try to really

hone in and see if there are things that need to be done to address those questions and let's move on with the legislation instead of engaging in an ongoing PR extravaganza.

I thank the chairman.

Mr. WAXMAN. The theme of this hearing is to get out the truth. That is why this hearing is being held and why we have witnesses before us to respond to questions that they have been unwilling to respond to in any other place, whether it has been from members of the press or from anyone else who is seeking to get that information which I think the public ought to have.

Mr. Wyden.

Mr. WYDEN. Thank you very much, Mr. Chairman.

First, let me say to the gentleman from North Carolina that we are here for one reason, and that is to save lives and help improve the health of the American people. The gentleman says that lawyers on this committee are all getting together to make judgments. What we are doing is following up on the recommendations of virtually every objective medical group in our country. We are not lawyers conducting medical inquiries. We are Members of Congress elected by our constituents to work on health care issues, and it seems to me when the Surgeon General, the American Medical Association and the World Health Association all say that we need these measures to improve the public health, we have an obligation as elected officials to follow up on what these health groups are saying.

Personally, I think it is high time that this committee investigates the pseudoscience that has been purveyed for years by the Council on Tobacco Research.

As we go to our witness, I would like to read what the Wall Street Journal had to say on this matter. They said, and I quote: "For almost 4 decades the Council for Tobacco Research in New York City has been the hub of a massive effort to cast doubt on the links between smoking and disease. Sponsored by U.S. tobacco companies and long run behind the scenes by tobacco industry lawyers, the ostensibly independent council has spent millions of dollars advancing sympathetic science. At the same time it has sometimes disregarded or even cut off studies of its own that implicated smoking as a health hazard."

Then they quote an employee named Dorothea Cohen, who worked there for 24 years saying and I quote: "When the Center for Tobacco Researchers found out that cigarettes were bad and it was better not to smoke, we didn't publicize that in press releases." She goes on to say, "The Council for Tobacco Research is just a lobbying thing. We were lobbying for cigarettes."

So I for one think it is high time we find out exactly what this organization does. It seems to me when the Wall Street Journal—not exactly an organ of antibusiness opinion—talks about the activities of this organization in the fashion I have described, it is our obligation as public officials to pursue it.

I yield back my——

Mr. WAXMAN. Rather than yield back your time, would you yield to me?

Mr. WYDEN. I would be happy to.

Mr. WAXMAN. You made reference to a seminal article in the Wall Street Journal about how cigarette makers keep health questions open year after year. The Council for Tobacco Research was the subject of that article.

This article cited the Council for Tobacco Research as refusing to answer any questions. They refused to answer questions for the Wall Street Journal, New York Times, any of the representatives of the press in this country that gives out information to the public.

Well, I think they should be called before the Congress of the United States to give out the information that I think is appropriate for us to know about their activities and their presumed scientific inquiries—whether it is genuine science or public relations science, whether they are engaged in what they say they are supposed to do, which is to pursue the truth, or whether they are trying to lay a veil of secrecy over that truth.

I do want to point that out. The press can't insist on these answers but the Congress of the United States will insist on answers to these important questions.

Mr. Greenwood.

Mr. GREENWOOD. No, thank you, Mr. Chairman.

Mr. WAXMAN. We will leave the record open for other members of the subcommittee who wish to insert statements in the record.

Mr. WAXMAN. Our witness this morning is Dr. James Glenn, chairman and CEO and president of the Council for Tobacco Research.

Dr. Glenn, as is our custom in tobacco control hearings, we would like to swear in all witnesses. I want to tell you that at the desk next to you are the applicable Rules of the House, and the Rules of the Committee. They will inform you of the limits on the power of this subcommittee and the extent of your rights during your appearance today.

Do you or those who will accompany you desire to be represented by counsel or advised by counsel during your appearance here today?

Mr. GLENN. Perhaps so, Mr. Waxman.

Mr. WAXMAN. Well, you are entitled to be represented by counsel. I want to inform you of that fact.

Do you or those who you have asked to accompany you object to appearing before this subcommittee under oath.

Mr. GLENN. No, sir.

Mr. WAXMAN. If you have no objection, I would like to ask you to rise and raise your right hand.

[Witnesses sworn.]

Mr. WAXMAN. Please consider yourself to be under oath and identify yourself for the record and proceed with your testimony.

TESTIMONY OF JAMES F. GLENN, CHAIRMAN, COUNCIL FOR TOBACCO RESEARCH, USA

Mr. GLENN. I am Dr. James F. Glenn. I am a surgeon. I am chairman, president and chief executive officer of the Council for Tobacco Research, USA.

I am pleased to be here and happy to cooperate with this committee in their investigations. I am even more pleased to be able

to bring to public record the facts and the truth about the activities of the Council for Tobacco Research.

By way of personal introduction, I am a native of Kentucky. I had my undergraduate education at the University of Rochester. I received my medical degree from Duke University. I have postgraduate training in general surgery at Harvard in the Peter Bent Brigham Hospital. I subsequently had neurologic training at Duke University after completing a tour as a flight surgeon during the Korean War.

I served on the faculty at Yale University, Bowman Gray University, and for 18 years I was chairman of the Urology Department at Duke University Medical Center. I then served as dean of the medical school at Emory University in Atlanta and then as president of Mount Sinai Medical Center, Mount Sinai Hospital and Mount Sinai Medical School in New York.

For the past 7 years, I have been associated with the Council for Tobacco Research, also serving simultaneously on the faculty of the University of Kentucky, first in the capacity of director of the Lucille P. Markey Cancer Center at that institution, and currently as chief of staff of the University Hospital and dean for Clinical Affairs.

My curriculum vitae and bibliography are available to you and I will be happy to answer any questions about that, but I thought I would not belabor that.

I am, of course, certified by the American Board of Urology. I am a member of some 35 professional organizations. I am currently president of the International Society of Urology, and I have served as president of the Southeastern Section of Urology, the American Association of Genitourinary Surgeons, president of the Clinical Society of Genito-Urinary Surgeons, president of the Society for Pediatric Urology, president of the Society of Pelvic Surgeons, and other associations.

I have authored one of the best selling textbooks in urology and I have some 270 publications in my bibliography, which is before you.

I joined the Council for Tobacco Research in 1987 at their invitation first as a member of the Scientific Advisory Board then as their assistant scientific director, subsequently as scientific director, and I am currently chairman, president, and CEO of the organization.

There has been recently a great deal of negative press about the Council for Tobacco Research. We have been accused of being a public relations ploy for the tobacco industry. We have not responded to many of these inaccuracies in the press because we didn't want to appear as a public relations arm.

It has been said that we have concealed research from the public and provided misinformation about tobacco use and disease. Quite the contrary.

Indeed, I reject both of those implications. As this hearing progresses, I hope to demonstrate to you that the activities of the CTR have been open and aboveboard at every turn.

The Scientific Advisory Board does not consider whether research results will be favorable or unfavorable to the tobacco industry. We are scientists and we seek scientific truth.

We encourage independent investigators to publish their results in reputable journals, preferably peer-reviewed. The industry exercises no control over our activities, over the granting of funds for basic research, or the sort of research that will be pursued.

The Council has never diverted any research into special programs or special projects for the purpose of suppressing research.

Those who have worked with the Council over the years, as I have, recognize these allegations to be untrue. Let me try to give you some facts to replace these erroneous speculations.

The Council is a private, nonprofit organization that sponsors research into questions of tobacco use and health. It was founded in 1954 as the Tobacco Industry Research Committee, later changing its name to the current one.

It has been funded primarily by the five major tobacco manufacturers over the years. The awards are approximately $20 million per year at the present time, making the Council for, CTR one of the largest private granting agencies in the Nation. We have awarded over $220 million over the years, funding some 1,380 projects by about 1,000 biomedical investigators. All this research has been performed by independent scientists.

The Council for Tobacco Research does not accomplish research on its own. We have no research facilities. We are simply a funding agency for independently accomplished private research.

The funded research has been done at preeminent medical institutions throughout this country and abroad. We have grants at Harvard university, Johns Hopkins, Duke University, the University of Texas, the Mayo Clinic, Scripps Research Institute, the National Institutes of Health, and several Veteran's Administration hospital facilities.

A large number, perhaps the overwhelming majority of the research projects that we have funded, have been co-funded by other distinguished granting agencies including the National Institutes of Health, and its National Cancer Institute, also by the Environmental Protection Agency, the American Cancer Society, the American Lung Association, and the American Heart Association.

I am sure if you have perused the 30 copies of the annual reports that we have provided for you you will see the nature of the research and also the credits of those efforts both to the CTR and simultaneously to other agencies.

The funding is provided for research in certain key biomedical areas. Cancer leads the list. Over half of our grants at the present time are devoted to some aspect of malignant disease. Cardiovascular diseases have played an important role. We are supporting research in cellular and molecular biology and developmental biology.

Epidemiology has been an interest, though fading, because epidemiologic studies are not at the cutting edge of science any longer.

We are progressively funding research into areas of genetics, immunology, the neurosciences, and I might mention that currently we are sponsoring a conference here in Washington, DC., which is under the auspices of the New York Academy of Sciences and it deals with the functional diversity of interacting receptors. This conference is a special conference of the New York Academy.

Our sponsors were willing to add additional funds to our research fund in order to sponsor this conference. It is now in its second day here in this city. It is comprised of some of the most distinguished neuroscientists in the world.

Our focus has been on basic research. In recent years all medical research has focused on the macroscopic to the microscopic. We are now down to the cellular and molecular level as the basis for disease. Until we understand the mechanisms that can induce cell regulation and deregulation, we cannot answer the fundamental question of what causes cancer, for example.

We believe that we are providing the best opportunity for understanding the processes and mechanisms of disease, specifically those that are statistically associated with smoking. This program is consistent with that of other granting agencies such as the NIH, American Heart Association, American Cancer Society.

Our grantees who are a broad spectrum of basic biomedical scientists for the most part are assured complete scientific freedom in conducting these studies. The grantees alone are responsible for publishing their results. We do not publish papers. We do publish an annual report with abstracts of all of the papers published by our grantees. This is done as a summary and a service to the biomedical community, and you have that information available to you.

The grantees in general are encouraged to publish in peer-reviewed journals and publication is encouraged in every instance. We have never suppressed publication of any articles.

There are more than 5,000 basic biomedical contributions in the literature reporting results of CTR sponsored research. They are in the most respected journals, and I will be glad to list those for you, if you so desire.

Now, how does the CTR function? The CTR functions very much like a study contribution of the NIH, and I speak from personal experience in telling you this.

We have a Scientific Advisory Board of 15 very distinguished biomedical scientists from all over this country and Canada. Applicants are encouraged to submit to us a preliminary inquiry trying to determine whether we would have an interest in supporting their research efforts.

These preliminary inquires are reviewed by members of the Scientific Advisory Board. In general, about 50 percent of the preliminary inquires are encouraged to be resubmitted as full grant applications.

When the full grant application is submitted, the Scientific Advisory Board members review these. All members of the Scientific Advisory Board review all grants and two or more of the Scientific Advisory Board are asked to submit written reports regarding these grants. Then twice yearly the Scientific Advisory Board gathers for a day session during which they rank and score these grant applications.

Clearly, we are not able to support all of the good research that is submitted to us, but we do fund grants to the extent of 12 percent of the submissions. This is approximately the same as the funding level at the National Institutes of Health at the present time.

I hope that some of this has served to dispel any unwarranted suggestions about the Council. I am particularly disturbed that your source of information is the Wall Street Journal. The article is totally misrepresentative of our activities. I have been asked why we did not respond to the Wall Street Journal. The simple answer is, where would we start?

So many inaccuracies are included in that article that it would be impossible for us to make an appropriate and full defense.

I am proud of the Council for Tobacco Research. Our record is a very distinguished one, as you will be told by representatives of other granting agencies. We rank with the major private funding organizations of the Nation in supporting independent research by outstanding investigators. There have been a number of breakthroughs that have occurred as a result of our research, and I will be happy to list those for you, if you would like to hear about them. Basically I think I could mention three.

We supported Dr. Stanley Cohen, subsequently a Nobel Laureate in the identification of the epithelial growth factor as a key to understanding cell regulation.

We supported also Dr. Alfred Knutson, the man who first developed the two hit theory of the development of cancer. This led to the identification of the gene that causes the lethal retinal blastoma cancer of the eye in children.

We supported Dr. Henry Lynch for many years in developing his genetic library, library of familial cancers. Dr. Lynch and his library were the linchpin, if you will, in the recent work accomplished at Johns Hopkins in identifying the nonfamilial nonpolykosis colon cancer gene. A major breakthrough in our understanding of the genetic basis of disease.

I am very proud of the work of the Council for Tobacco Research. I am proud of my association with it. I am proud of what we do. I am proud of our staff and of the fact that the industry has chosen to support this independent research activity.

Thank you very much. I am happy to cooperate and will be pleased to answer any questions that you might have.

[Testimony resumes on p. 357.]

[The prepared statement and grantee institutions of Mr. Glenn follow:]

THE COUNCIL FOR TOBACCO RESEARCH-U.S.A., INC.

SUPPORTING BIOMEDICAL INVESTIGATION

Testimony of James F. Glenn, M.D.

As Chairman, President and Chief Executive Officer of The Council for Tobacco Research -- U.S.A., Inc., I am pleased to be here today at your invitation to testify about the Council's research program. Before describing for you the contributions the Council has made to the progress of scientific knowledge about diseases associated with smoking, I would like to provide some information about myself.

Personal Background

I received a Bachelor of Arts Degree in General Science from the University of Rochester in 1950. I then attended Duke University School of Medicine, receiving a Doctor of Medicine degree with honors within three years. From 1952 to 1954, I was trained in general surgery at Peter Bent Brigham Hospital in Boston. After serving in the army as a Captain and Flight Surgeon, I returned to Duke University in 1956, where I was Assistant Resident and then Chief Resident in Urology.

In 1959, I became an Assistant Professor of Urology at Yale University School of Medicine. From 1961 to 1963, I was an Associate Professor of Urology at Bowman Gray School of Medicine. In 1963, I was appointed Professor of Urology and Chief of the Department of Urology at Duke. I

remained at Duke until 1980, when I became Dean of the Emory University School of Medicine in Atlanta, where I was appointed Professor of Surgery. In 1983, I left Emory to become President of Mount Sinai Medical Center in New York City, where I also served as Acting Dean at the Mount Sinai School of Medicine from 1983 to 1984 and as Professor of Urology. In 1987, I returned to my roots, joining the University of Kentucky College of Medicine as Professor of Surgery. Between 1989 and 1993, I served as the Executive Director of the University of Kentucky Medical Center's Markey Cancer Center. In 1993, I became Chief of Staff of the University of Kentucky Medical College Hospital, a position I continue to hold.

I am certified by the American Board of Urology and am a Diplomate of the National Board of Medical Examiners. I am licensed to practice medicine in Kentucky, Connecticut, South Carolina, North Carolina, Georgia and New York.

I am a member of 35 professional organizations, including the American College of Surgeons, the American Surgical Society and the American Urological Association. Among the various positions I have held in professional organizations are President of the International Society of

Urologic Surgeons; President of the American Association of Genitourinary Surgeons; President of the Clinical Society of Genito-Urinary Surgeons; President of the Society for Pediatric Urology; President of the Society of Pelvic Surgeons; and President of the Society of University Urologists. I have authored or co-authored over 270 publications in medical journals, as well as numerous chapters in medical textbooks. Attached to my statement is a copy of my curriculum vitae, which lists the honors I have received and further detail about my professional experience, as well as a bibliography listing my publications.

I became associated with the Council for Tobacco Research in 1987, when I was invited to join the Scientific Advisory Board and to serve as the Council's Assistant Scientific Director. In 1988, I became the Scientific Director, a position I held until 1991. I became the Council's Chairman and CEO in 1991, and assumed the additional role of President on January 1, 1993.

As the head of the Council, I have responsibility for the Council's budget, which includes both grants and operating expenses, and for assuring that the Council's

staff, the Scientific Advisory Board and the Council's grantees are fulfilling their respective responsibilities.

The Council and Its Mission

The Council is a private, non-profit organization that sponsors research into questions of tobacco use and health and makes the results of that research available to the public. The Council is funded primarily by five tobacco manufacturers. The Council currently awards approximately $20 million a year in grants-in-aid to assist biomedical research, making it one of the largest private grant-giving organizations funding scientific research in the United States today.

The Council uses its funds to support established experts as well as promising new researchers at universities and medical centers in the United States and abroad. All of the research funded by the Council is performed by independent scientists. The Council does not itself operate any research facilities.

The Council and its predecessors have awarded in excess of $220 million to fund over 1,380 projects performed by approximately 1,000 researchers. Our grantees include three Nobel Prize laureates. A substantial portion of the researchers receiving Council grants have received co-

funding from both governmental and non-governmental entities, such as the National Institutes of Health (including the National Cancer Institute), the Environmental Protection Agency, the American Cancer Society, the American Lung Association, the American Heart Association and other leading sponsors of medical research.

The Council has funded research at most of the preeminent medical and scientific research institutions in the United States, including Harvard Medical School, Johns Hopkins University, MIT, Yale University, Stanford University, the University of Chicago, Columbia University, Princeton University, the University of Texas, the Mayo Clinic, Scripps Research Institute, the American Red Cross, the Salk Institute, the National Institutes of Health and several Veterans Administration Hospitals, to name but a few. Attached to my statement is a list of institutions that have received grants from the Council.

The Council funds grants in a variety of biomedical fields, including cancer, cardiovascular diseases, cell biology, developmental biology, epidemiology, genetics, immunology, neuroscience, pharmacology, pulmonary diseases, radicals and virology. The investigations that have received Council grants have varied over time as the

direction of scientific research has changed. In earlier years, in addition to funding other research areas, the Council funded epidemiological studies, animal inhalation studies, cell culture research, basic clinical research and pathology studies. The Council has also sponsored conferences on various areas of research, such as animal inhalation and cell cultures. In more recent years, the Council's focus has been largely on basic cellular and subcellular research, which today is believed to provide the best opportunity for understanding the processes and mechanisms of diseases, including those that have been statistically associated with smoking. The Council's increasing allocation of grants to basic research reflects the progress of science generally and is consistent with the evolution of research programs at other funding agencies concerned with questions of tobacco use and health, such as the National Institutes of Health, the American Heart Association and the American Cancer Society.

The Council's financial support has been an important resource for independent research that advances knowledge about tobacco and health. It has sponsored pioneering work in identifying familial cancers, the role of genetic factors in cancer formation, and the identification

of oncogenes. The Council was instrumental in supporting early work on the role of free radicals in the etiology of diseases and in opening up the new field of growth factor research. This work, like the rest of the research supported by the Council, has added to the scientific knowledge of the mechanisms and processes of diseases statistically associated with smoking.

Council grantees are assured complete scientific freedom in conducting their studies. They alone are responsible for reporting their findings in the accepted scientific manner -- through medical and scientific journals and societies. Publication of research results is encouraged in all instances. That Council grantees respond to this encouragement is attested to by the more than 5,000 publications that have appeared reporting the results of the Council-funded research projects undertaken by its 1,000 grantees. Those articles have appeared in the most respected peer-review journals, including the Journal of the National Cancer Institute, the Journal of the American Medical Association, the New England Journal of Medicine, and the journals Cancer, Heart and Circulation. The Council also prepares and distributes an annual report that contains

abstracts of publications appearing during the year that resulted from research funded by the Council.

The Council has also, to my understanding, contracted with investigators to undertake research projects on specific matters that involved larger and longer-term commitments than was normally available through the grant program. In addition, I understand that the Council in the past administered funds for special projects that particular companies had separately arranged for investigators to perform; these special projects were not part of and did not impact the Council's grant program. Nor to my knowledge is there any truth to the notion that such special projects were used to suppress the publication of research results.

Procedures for Awarding Grants

The Council's grant-review process is similar to that used by many other granting agencies, such as study sections of the National Institutes of Health. Funding decisions by the Council are made upon advice received from its Scientific Advisory Board ("SAB"). The SAB is composed of distinguished scientists from various fields of biomedical research. With the exception of the Scientific Director, who is a full-time Council employee, SAB members retain their affiliations with their academic and research

institutions. There are currently 15 SAB members, including three members of the National Academy of Sciences. The SAB members receive a per diem allowance in connection with attending meetings, but they are not compensated for the much more substantial time they spend reviewing applications between meetings. The SAB has an Executive Committee, which consists of the Chairman and Vice-Chairman of the SAB, the Scientific Director and three other SAB members.

The grant process begins with the receipt of a proposal from an applicant. Independent investigators send preliminary applications to the Council, describing their proposed research. The preliminary applications are read by several members of the Executive Committee of the SAB. The Executive Committee then votes to encourage or discourage the application.

Final, full applications are distributed to all members of the SAB. Each final application is also assigned to two members of the SAB selected on the basis of their knowledge and expertise in the relevant scientific field. These reviewers are given primary responsibility for evaluating the proposal in detail and presenting it to their SAB colleagues. The SAB meets twice a year to discuss the applications and to rate them by secret ballot. The SAB's

ratings are then used to establish a priority ranking among the applications, which I, in consultation with the Council's scientific staff, apply in allocating specific grant awards. The SAB is informed of the precise awards made by the Council.

Most grant applications request a three-year period of support. Grants are awarded, however, for one year at a time. For the second and third years of a typical grant, the researcher must submit what we call a noncompeting renewal application. These applications are reviewed by two SAB members -- generally the same two SAB members who were the principal reviewers of the original grant application. The full SAB then votes whether to recommend the applications for approval.

Some applications for grant support involve areas of inquiry about which SAB members believe they would benefit from consultation with experts and specialists outside of the Council in considering applications. In those occasional instances, members of the SAB recommend to the Council's scientific staff scientists or physicians who are knowledgeable on the particular subject; these individuals are then asked to assist in reviewing the grant

application. These scientists are selected because of their distinguished credentials and their particular expertise.

If, after the completion of the typical three-year grant cycle, a researcher wishes to receive further support from the Council for an extension of the same research project, he or she must submit a competing renewal application. Competing renewal applications are evaluated through the same process by which full original applications are evaluated.

In evaluating grant applications, the members of the SAB bring to bear their understanding of the state of scientific knowledge in the areas covered by the grant proposals. The SAB members consider the results of previously reported research in any particular field, which might include research performed by Council-funded investigators, in evaluating whether a particular proposal is meritorious.

The SAB does not consider, for any type of grant application (original, noncompeting renewal or competing renewal), whether any of the investigator's prior research produced results thought to be favorable or unfavorable to the tobacco industry. Industry sponsors exercise no control over the decision to fund a particular grant application or

with respect to the publication of the results of any sponsored research.

Selection of SAB Members and Other Peer Reviewers

The Council selects for the SAB distinguished scientists who can bring cutting-edge expertise in various areas of biomedical research. The Council seeks to maintain a wide range of expertise on the SAB, so that the appropriate biomedical areas are represented in the grant application process.

When a vacancy occurs on the SAB, the Chairman of the Council and the Scientific Director solicit from SAB members recommendations for a successor. As a general matter, the Chairman of the Council or an SAB member will contact individuals who have been recommended and ask them to attend an SAB meeting to give a presentation on their research. After candidates have attended an SAB meeting, SAB members and the Chairman of the Council will confer to see if there is a consensus to extend an invitation to join the SAB.

* * * * *

I am proud of The Council for Tobacco Research and my association with it. The Council has provided vital support to nearly 1,000 independent researchers. Its research program has played a key role in advancing our knowledge of diseases that have been associated with smoking. I thank the Subcommittee for this opportunity to present this brief picture of the Council and its contributions to biomedical research, and I am happy to answer any questions you may have.

Mr. WAXMAN. Dr. Glenn, thank you very much for your testimony and for being here today.

I appreciate your being here and since you are our only witness, if you need to take a short break at any time, let us know.

We are going to go through some areas and give you the opportunity to respond to some of these things that have been said and tell us more information about the Council on Tobacco Research.

I find your comments about the Wall Street Journal article interesting. You didn't comment to them before they did the article and then afterwards they had so many inaccuracies you didn't want to respond.

This is your chance and we want to go through some of these issues with you.

In recent months, we have begun the process of learning more about the tobacco industry. We still, however, need to know more about this Council on Tobacco Research. I want to go back over 40 years.

In 1954, the major tobacco companies joined together in issuing a "frank statement to cigarette smokers", a copy of this statement is Exhibit 4, and excerpts of the statement are displayed on the chart, which we would like to have displayed.

Are you familiar with this statement?

Mr. GLENN. Yes, sir.

Mr. WAXMAN. You know at the same time the companies created the Tobacco Industry Research Council, the previous name for your Council for Tobacco Research.

Mr. GLENN. Yes.

Mr. WAXMAN. I released the staff report today on Hill and Knowlton documents, which were written from 1954 to 1956. These documents provide considerable insight into the founding of your Council, and I would like to ask you some questions about these documents.

In 1953, there was tremendous public interest in the hazards of smoking. In that year, for instance, Dr. Winter of Sloan-Kettering published a major study showing that mice painted with tobacco tars developed fatal cancers. A copy of this report is Exhibit 1.

The Sloan-Kettering report received significant public attention at the time. Are you aware of this report?

Mr. GLENN. Yes, sir.

Mr. WAXMAN. The tobacco industry was very concerned about the Sloan-Kettering report and other similar work coming out in the early 1950's. In fact, on December 15, 1953, an unprecedented meeting of the CEO's of the major tobacco companies took place to respond to these reports. Are you aware of that meeting?

Mr. GLENN. Yes, sir.

Mr. WAXMAN. I have a memorandum written by Bert C. Goss of the public relations firm Hill and Knowlton as Exhibit 2. Mr. Goss and the founder of Hill and Knowlton, John Hill, attended the December 15 meeting. Mr. Goss' memorandum memorialized what happened. Are you familiar with his memorandum?

Mr. GLENN. I think I am, Mr. Waxman.

Mr. WAXMAN. This memorandum is crucial in understanding the strategy of the tobacco industry. In attendance at the meeting were Paul Hahn, president of the American Tobacco Company; Joseph

Cullman of Benson & Hedges; Parker McComas, president of Philip Morris; Whitney Peterson, president of U.S. Tobacco.

According to the memorandum, the meeting is the first time these CEO's ever met out of a social context. They are taking this extraordinary step because they agree that the health criticisms are extremely serious and worthy of drastic action.

At the meeting they agreed that what is needed is not more science or research but a public relations campaign to counter the mounting evidence of the adverse health effects of smoking. In their own words they decide they should sponsor and I quote, "A public relations campaign which is entirely pro-cigarettes."

The plan of action is fleshed out in another Hill and Knowlton memorandum written just 9 days later. This is Exhibit 3, entitled "Preliminary Recommendations for Cigarette Manufacturers."

In this memorandum, Hill and Knowlton recommends that your organization be created for explicitly public relations nonscientific purposes. Are you familiar with this exhibit?

Mr. GLENN. No, sir.

Mr. WAXMAN. The memorandum states and I quote, "The underlying purpose of any activity at this stage should be reassurance of the public...It is important that the public recognize the existence of weighty scientific views which hold that there is no proof that cigarette smoking is a cause of lung cancer."

The memorandum goes on to recommend that to achieve this public relations purpose, the industry should create the Council for Tobacco Research—then called Tobacco Industry Research Committee; and the memorandum further recommends that the very first action of the new organization should be the assurance of a frank statement, like that we talked about earlier.

As you can see, your organization was not thought up by scientific researchers who perceived a need to know more about health effects of tobacco, it was dreamt up by the public relations experts who perceived the need to calm public fears.

It is not fair for me to ask you if you are familiar with all the documents in this subcommittee report. You have not had a chance to study them all thoroughly. Instead, I want to describe for you some of the early activities of the Council for Tobacco Research. I will describe these activities and ask you a simple question, are these activities scientific in nature—as you say is the devotion and goal of the Council—or are these public relations activities?

Let me begin with a simple matter of staffing.

According to these documents, the Council for Tobacco Research hired 23 public relations experts from Hill and Knowlton in 1954, its first year of operation, and 35 public relations experts from Hill and Knowlton in 1955, which would be its second year of operation.

Can you explain why a small organization that is supposed to be purely scientific needs to employ the services of 2 to 3 dozen public relations experts?

Mr. GLENN. Mr. Waxman, on the basis of my knowledge I would have to reject that. The Council for Tobacco Research has been the research arm not the public relations arm for the tobacco industry.

Mr. WAXMAN. Well, we have Exhibit 10 which shows the budget of the organization at that time. It indicates the charges paid to

Hill and Knowlton, which of course no one would argue is a scientific organization. This was before you were there at the Council.

At that time, they were spending money on 2 to 3 dozen public relations experts. According to these documents, one of the activities of the Council was to turn obscure research findings that were favorable to the tobacco industry into headline news around the country.

A good example of this is Exhibit 13, a confidential public relations report on the activities of the Council and I want to read to you from page 6 of this report. "A report from the New Zealand public health official, published in a British medical journal, attributed the increase in lung cancer incidence to air pollution and not to smoking. Advance information of the date of publication was obtained from contacts in New Zealand and England when it appeared and it was brought to the attention of the United States press. Stories and editorials on it appeared in many newspapers."

Dr. Glenn, is this activity, encouraging the media to write stories about obscure research favorable to the tobacco industry, a scientific activity or public relations activity?

Mr. GLENN. Mr. Waxman, my answer to that, I have to tell you that in 1954 I was in the Korean War as a flight surgeon so I may not be au courant with what was happening in the press at that time.

I will say that these documents were not made available to me until this young man began passing them here to the witness table. So I really haven't had a chance to review them and I have had no opportunity to develop any response.

This is ancient history and I really cannot verify it one way or the other.

Mr. WAXMAN. Well, I am asking you from the documents I have described, and I have acknowledged the fact that you were not there, if the Council were working on encouraging writers of newspapers to cite obscure scientific articles and they were trying to get favorable articles written, would you consider that, what I have just described, as scientific research activity or public relations activity?

Mr. GLENN. I appreciate the way that you have phrased the question. I was not there. But I can tell you that the Council for Tobacco Research and its research arm have been directed by a Scientific Advisory Board of very distinguished people from the beginning.

Mr. WAXMAN. But I am asking you to answer for me whether you consider the activity I described for you scientific in nature or public relations in nature?

Mr. GLENN. Mr. Waxman, the activities of the Scientific Advisory Board and the Council for Tobacco Research have always been dedicated to science.

Mr. WAXMAN. Let me——

Mr. GLENN. Whatever activities that may have been accomplished by Hill and Knowlton are beyond my knowledge or recollection.

Mr. WAXMAN. Hill and Knowlton was paid a substantial amount of money by the Council. According to these documents, another activity of the CTR was to commission free-lance authors to write fa-

vorable articles about cigarettes. These articles would then apparently be published under the name of the free-lance author with no acknowledgment of the link to the Council.

For instance, Exhibit 9, a report on tobacco industry research committee information activities contains this entry on page 4, "C.B. Colby, free-lance popularizer of science was retained for research and possible writing of articles concerning all the hazards of modern life which people are cautioned against and leading to the conclusion that in spite of all the death scares, you still live longer."

Is hiring a free-lance popularizer of science urging people to ignore death scares a scientific inquiry?

Mr. GLENN. That is beyond my knowledge, as you must know. I notice this memorandum, however, is an internal memorandum of Hill and Knowlton. They, indeed, are a public relations firm. But they were independent of and separate from the Council for Tobacco Research to my knowledge.

Mr. WAXMAN. I dispute that.

We will move on to other Members who have questions and we will come back to some of these points.

Mr. Bliley.

Mr. BLILEY. Dr. Glenn, could you identify those who serve on the CTR Scientific Advisory Board, what their background is?

Mr. GLENN. Yes, sir. Let me go to my notes lest I miss somebody. The Scientific Advisory Board consists of at the present time 15 very distinguished individuals; alphabetically they are, Dr. Leo G. Abood, professor of Pharmacology and Biochemistry at the University of Rochester; Dr. Barry G. Arnison, chairman of the Department of Urology and director of the Brain Institute at the University of Chicago; Dr. Drummond Bouden, chairman of the Department of Pathology, University of Manitoba; Dr. Michael Brennan, director emeritus of the Michigan Cancer Center in Detroit; Dr. Carl O. Croci, director of the Thomas Jefferson Cancer Center, Thomas Jefferson University, Philadelphia; Dr. Raymond Erickson, professor of Molecular Biology, Harvard University; Dr. Joseph Feldman, professor of Immunology and research director emeritus at the Scripps Institute in California; Dr. Gordon Gale, professor of Medicine and Endocrinology at the University of California, San Diego; Dr. W. K. Yaclick, professor and chairman of the Department of Microbiology at Duke University; Dr. Manfred Carnofski, professor of Biochemistry, Harvard University; Dr. Henry Lynch, Creighton University, director of the Department of Preventive Medicine, and the same Lynch to whom I referred previously who is responsible for our most recent understanding of genetic disease for—as the basis for cancer; Dr. Harmon McAllister, a biochemist and our current scientific director, also a member of the board; Dr. Barry Pierce, chairman emeritus of the Department of Pathology, University of Colorado; Dr. Judith Swain, professor of Medicine, director of the Division of Cardiovascular Disease and Medical Genetics at the University of Pennsylvania; and Dr. Peter Vote, formerly chairman of the Department of Microbiology at the University of Southern California, now director of research at the Scripps Institute.

Mr. BLILEY. Isn't the role of the CTR's Scientific Advisory Board comparable to the role of similar advisory boards?

Mr. GLENN. Yes, sir.

Mr. BLILEY. To your knowledge to what extent have the member companies attempted to influence the research activities of the Scientific Advisory Board?

Mr. GLENN. They have never attempted to influence our activities in any way to my knowledge.

Mr. BLILEY. How long have you been in your present capacity?

Mr. GLENN. In my present capacity 5 years, 4 years, but associated with CTR for 7 years.

Mr. BLILEY. There have been some recent criticisms of CTR largely arising from the Cipollone case. Before the plaintiff's lawyers and the media began their criticisms, there was an interesting article that appeared in the July 1985 edition of the New York State Journal of Medicine, the article quoted among others, Joanne Shellenback, the Director of Press Relations with the American Cancer Society in New York.

She said of CTR and I quote, "They are legitimate. We are very critical of the tobacco industry in terms of their advertising practices and many of the things that they do but here is an area where they seem to be doing something by the book in promulgating good research. So I can't criticize them across the board."

Do you think that CTR has been unfairly criticized recently?

Mr. GLENN. Yes, sir, and I think it is by inference that we are supporting smoking which is certainly the furthest thing from the truth. We are an independent agency, we have the respect of medical investigators and institutions across the country and throughout the world. We are regarded as a good source of funding particularly for young people with fresh new ideas and approaches to the questions of basic biomedical investigation that are so fundamental to our understanding of cancer, cardiovascular disease, and others.

I think the statement from the American Cancer Society is entirely in keeping with the reputation we hold in the medical community.

Mr. BLILEY. You mentioned in your written oral statement that three researchers funded in part by CTR have received Nobel prizes in physiology on medicine. Could you name them?

Mr. GLENN. Yes, sir. I think I mentioned Dr. Stanley Cohen of Vanderbilt University for his work with epithelial growth factor. The second was Dr. Barry Nazerath of Harvard University, who really was the father of modern molecular biology. And the third Nobel prize winner was Dr. Harold Varmus, currently the Director of the National Institutes of Health.

Mr. BLILEY. Beyond the three researchers funded in part by CTR that have received Nobel prizes, can you give this subcommittee some idea of the quality of the research which has been funded by CTR?

Mr. GLENN. Well, I think the quality speaks for itself. As you peruse the annual reports you will see that we have moved to the cutting edge of basic biomedical research. I think the quality is tested by some of the examples I gave in my opening statement of individuals who have made major breakthroughs in our understanding of basic disease process.

However, you must understand that our review process and the selection of grantees to be supported is a very critical mechanism. We receive well over 1,000, close to 1,200, inquiries and applications per year. We are able to fund only a minute portion of those total inquiries and applications. So we are really—we really are picking the cream of the crop it would seem. I think our judgment has been borne out by the succession of the investigators.

Mr. BLILEY. What is the publication policy of CTR?

Mr. GLENN. We encourage all investigators to publish everything that they wish to publish. We have never discouraged publication. I would cite as an example the fact that we were approached by Dr. Edward Campbell of the University of Utah recently. Dr. Campbell is one of our grantees and he is working on the problem of emphysema.

He has identified a genetic defect that leads to an alpha 1 antitrypsin deficiency and in those individuals perhaps representing some 3 to 5 percent of patients with emphysema, this enzyme deficiency predisposes them to emphysema.

He inquired of us whether he should publish these results, and we said, most certainly you should publish those results. Those are the individuals who are most susceptible to emphysema and certainly those who should be kept away from the risk factors such as smoking.

Mr. BLILEY. There has been recent criticism that the research funded by CTR doesn't have anything to do with cigarette smoking and health. Does your experience support this criticism?

Mr. GLENN. No, sir, we are supporting very fundamental research into molecular and cellular biology, genetics and immunology which are the fundamental questions that must be answered before we can address questions of therapy and social habits.

Mr. BLILEY. It has been claimed that research has been channeled or funneled into CTR special projects so that adverse results could be suppressed from publication by claiming that they were subject to the attorney-client privilege.

I understand that many publications resulted from CTR special projects. I also understand that all of the privileged documents were reviewed by special master Joel A. Persono who was appointed by Judge Sarokin and who later became a United States magistrate judge. In the special masters report he states, and I quote, "The research projects themselves were conducted by independent scientists affiliated with a variety of academic and research institutions who were not applied by or related to the tobacco industry. These researchers were permitted to publish the results of their research with credit given to the CTR."

Is that consistent with your understanding?

Mr. GLENN. Yes, sir.

Mr. BLILEY. I also understand that some researchers who received CTR special projects funding were co-funded by other funding agencies and that a lot of this research was published in peer review journals and acknowledgment to special project support was requested; is that right?

Mr. GLENN. Yes, sir. I would point out that special projects were projects that were desirable for our sponsors. However, our scientific director reviewed these projects for scientific accuracy, for

methodology, and the CTR then served merely as the funding agency for such projects.

However, your first—initial statement is correct. Some 250 peer-reviewed articles were published as a result of the various special projects that were accomplished.

Mr. BLILEY. Some of what people are claiming here today doesn't make sense. If a researcher was being funded by both the Federal Government and a CTR special project grant, how could CTR prevent publication?

Mr. GLENN. We couldn't, Mr. Bliley. You can't prevent a biomedical investigator from doing anything he wants to do. He certainly will publish at his discretion. We wouldn't presume to tell him not to publish. On the contrary, we have encouraged publication.

Mr. BLILEY. Would you submit a list of publications and presentations which are believed to have resulted from CTR special projects for the research?

Mr. GLENN. Would I submit such a list?

Mr. BLILEY. Obviously, you can't do it today but the record will be open, and I am sure the Chairman will keep it open for that.

Mr. GLENN. It is available to you, Mr. Bliley. We have submitted our annual reports for the last 30 years, which I am sure that much of it to people who are in different professions and even to me on occasion must look like Greek, but I think if you will ask competent biomedical investigators, authorities in the field to review the research reported in these annual reports you will see the very high quality of the research that has been done.

Mr. WAXMAN. Will you submit to this committee for the record a list of all the research funded under the special projects?

Mr. GLENN. Yes, sir, we will cooperate with you in any way.

[The following information was received:]

As I explained in my testimony, Council Special Projects were research projects that the Council's sponsors wished to fund. Tr. at 46. These research projects were funded by the sponsors, and were administered by the Council, separately from the grant-in-aid program.

We have prepared a list of all Council Special Projects for which the Council has a file. That list includes the following information for each such project (where such information is available from the Council's files or from published sources): (a) the name of the principal investigator or investigators; (b) the institution or institutions with which the principal investigator or investigators were associated; (c) the title or subject matter of the Council Special Project; (d) the dates of funding of the Council Special Project; (e) the total amount of funding provided by the Council; and (f) a list of the publications that apparently resulted, or may have resulted, from the Council Special Project. Some of the publications identified on the list appear in the Council's Special Projects files; others have been collected from other sources. In a number of instances, it is not clear whether a particular publication resulted from Council Special Project funding.

My statement at the May 26 hearing that 250 peer-reviewed articles are believed to have resulted from Council Special Projects was based on my information about the number of publications that either were in the Council's files or have been collected from other sources. Several clarifications should be made to that statement. First, our list sets forth over 400 articles or presentations that resulted or may have resulted from Council Special Projects; so far, I understand, copies of about 250 of these articles or presentations have been obtained, and that understanding was the source of my statement at the hearing. Second, most but not all of these 250 articles or presentations were peer-reviewed. Third, abstracts relating to Council Special Projects publications were not included in the Council's Annual Reports.

We expect to provide this list to you promptly after we have reached an understanding with the subcommittee staff with respect to procedures for the subcommit-

tee's handling of such materials provided by the Council. In the interim, I respectfully request that this letter be included at pages 47 and 106 of the May 26 transcript.

Mr. WAXMAN. Thank you.

Mr. BLILEY. Thank you, Mr. Chairman.

Last question, Mr. Chairman, if I may.

I further understand the documents related to CTR special projects research including proposals, interim reports, final reports, and publications have been produced to plaintiff's counsel in discovery in some cases. Is that correct?

Mr. GLENN. That is correct.

Mr. BLILEY. Thank you, Dr. Glenn.

Thank you, Mr. Chairman.

Mr. WAXMAN. Thank you, Mr. Bliley.

Mr. Synar.

Mr. SYNAR. Thank you, Mr. Chairman.

Welcome, Dr. Glenn. Let me go back to something Mr. Waxman was questioning you about. The Wall Street Journal on Thursday, February 11, stated the Council's role has never been just research and it was largely a creature of Hill and Knowlton, the public relations firm. Do you deny that?

Mr. GLENN. Yes, sir.

Mr. SYNAR. How does that square with the fact that in a 1954 memo, Exhibit 10 in front of you—do you have it?

Mr. GLENN. Yes, sir. This is the first time I have seen it, Mr. Synar.

Mr. SYNAR. All right.

That is interesting, Dr. Glenn. Usually when you take over a corporation as someone who is going to run it, one of the first responsibilities is to learn the history of the corporation and to learn the corporation's inner workings over the years. You are telling us you have not taken that time to do that?

Mr. GLENN. Mr. Synar, I have taken over a number of organizations in my career and I am well aware of the procedure. This is a Hill and Knowlton internal document.

Mr. SYNAR. But it is from the founder of Hill and Knowlton to the chairman of the CTR.

The paragraph says, attached are budget estimates for operations of the Tobacco Industry Research Committee during the calendar year 1955, which would be the first year of its creation.

Then it goes into the next paragraph, as you can see, the budget for the staff operations provides for 35 different staff members of the Hill and Knowlton Corporation.

Now, doesn't that fly in the face of your answer to Mr. Waxman that the Hill and Knowlton operation was separate from CTR, since the budget shows that it was fully funded by CTR?

Mr. GLENN. Mr. Synar, I am not sure of the thrust of your question.

Mr. SYNAR. Were you——

Mr. GLENN. Hill and Knowlton documents are not in our files.

Mr. SYNAR. The point is Hill and Knowlton was basically CTR, were they not?

Mr. GLENN. No, sir, on the contrary from the beginning CTR was composed of independent scientists serving on a Scientific Advisory Board.

Mr. WAXMAN. If you would yield to me, that document was written to the head of the Council for Tobacco Research. I don't know why it wouldn't be in your files, but it was written by Hill and Knowlton to your committee and I presume paid for by the Council.

Mr. GLENN. Mr. Waxman, I think you are presuming a lot. This is a confidential memorandum internal to Hill and Knowlton. It mentions the CTR but it is not in our files and there was no way I can know that nor do I know who paid for this.

Mr. WAXMAN. This one does not indicate that it is confidential.

Mr. GLENN. I am sorry.

Mr. WAXMAN. It doesn't indicate——

Mr. GLENN. Are we looking at Exhibit 9?

Mr. WAXMAN. No, 10.

Mr. SYNAR. Exhibit 10.

Mr. GLENN. Again, I can't speak to this because I have never seen it until this moment, but it would appear to me to be a Hill and Knowlton internal document.

Mr. WAXMAN. Would you confirm for us that Mr. Timothy Hartnett was the chairman of the Council for Tobacco Research?

Mr. GLENN. I can't confirm that to you, no, sir.

Mr. WAXMAN. Have you ever heard of him?

Mr. GLENN. No, sir.

Mr. WAXMAN. You never heard of him. OK.

Mr. Synar.

Mr. SYNAR. Dr. Glenn, you are proud of your scientists on your board. Have any of these Nobel prize winners done research in the area of tobacco or how it affects health?

Mr. GLENN. The Nobel prize winners?

Mr. SYNAR. Yes, that serve on your board.

Mr. GLENN. The Nobel prize winners that I mentioned, Mr. Synar, are former grantees of the Council for Tobacco Research.

Mr. SYNAR. Let me move on. A review of the Council——

Mr. WAXMAN. Just before we go too far I do want to indicate for the record that the annual report, 1963-1964, from the scientific director of the Council for Tobacco Research indicates that Timothy V. Hartnett is the chairman, W. T. Howe is the executive director, and Clarence Cook Little is the scientific director.

Mr. GLENN. I was not aware of Mr. Hartnett. Doctor—Clarence Cook Little was the first scientific director, very distinguished man, president of the University of Minnesota, founded the Bar Harbour Library, credited with establishing the basis for fundamental laboratory animal research.

Mr. WAXMAN. I am sure Mr. Hartnett was also quite distinguished. He was chairman of the Council and did receive that memo from Hill and Knowlton.

Mr. Synar.

Mr. SYNAR. Dr. Glenn, answer my question, did any of these grantees, the Nobel prize winning crew, do research on tobacco and how it affects health?

Mr. GLENN. Mr. Synar, every one of them has done fundamental research to help us understand underlying disease process.

Mr. SYNAR. I didn't ask you that.

Mr. GLENN. I know you didn't ask me that, Mr. Synar, but what you asked me was very naive.

Mr. SYNAR. Did they do research in tobacco research and how it affects health, yes or no?

Mr. GLENN. Yes.

Mr. SYNAR. Will you provide that for the record? We would like to see it.

Mr. GLENN. I would be glad to provide the papers published by these Nobel prize winners.

Mr. SYNAR. In the area of tobacco and how it affects health.

[The following information was received. Documents referred to hereinafter in these responses have been retained in subcommittee files.]

As I testified on May 26, the Council has funded three investigators who have won Nobel Prizes: Dr. Baruj Benaceraff of Harvard University, Dr. Stanley Cohen of Vanderbilt University and Dr. Harold E. Varmus of the University of California at San Francisco.

Dr. Benaceraff, who was awarded the Nobel Prize in 1980, received a Council grant from 1972 through 1974 for investigating "Control of Specific Cellular and Humoral Immune Responses to Neoplastic and Non-neoplastic Tissues." Item A in the Appendix includes three publications acknowledging the Council's support of Dr. Benaceraff's research.

Dr. Cohen, who was awarded the Nobel Prize in 1986, received a Council grant from 1987 through 1993 for investigating "The Role of Lipocortin in the Cellular Response to EGF." Item B in the Appendix includes six publications acknowledging the Council's support of Dr. Cohen's research.

Dr. Varmus, who was awarded the Nobel Prize in 1989, received a Council grant from 1984 through 1986 for investigating "Functional Analysis of Cellular Oncogenes Activated During Tumorigenesis." Item C in the Appendix is a publication acknowledging the Council's support of Dr. Varmus' research.

As I explained to the subcommittee on May 26, the Council-funded research by these Nobel laureates was basic biomedical research aimed at improving our understanding of fundamental disease processes—which is the kind of research that is now believed to further scientific understanding of the effects of tobacco use on health. Dr. Benaceraff conducted pioneering research into the humoral immunological response of the host when presented, attacked or invaded by cancerous growths. His work has provided important insights into how regulatory mechanisms may operate in defense of the host organism. Dr. Cohen studied cell growth factors and their role in regulating growth and differentiation. His investigation of genetic controls of growth factors opened the door to our understanding of mechanisms by which normal cells become cancerous. Dr. Varmus' pioneering work with oncogenes made important contributions to our overall understanding of how healthy cells become transformed into cells that can no longer control their growth and therefore become cancerous.

Mr. GLENN. Mr. Synar, one does not have to specifically investigate tobacco as a product——

Mr. SYNAR. Dr. Glenn, you just said under oath that they did have expertise in research in tobacco and health-related issues with respect to tobacco. Is that correct?

Mr. GLENN. Fundamental understanding of basic cellular and molecular biology is the basis for understanding scientific truth which will then let us understand the specifics of a vehicle such as tobacco.

Mr. SYNAR. That is a very convenient way to say that they are not conducting tobacco-related research, isn't it, Dr. Glenn?

Mr. GLENN. No, Mr. Synar, it is not.

Mr. SYNAR. Let's go on to the review of the Council for Tobacco Research published in the July issue of the American Journal; Exhibit 19, if the staff will provide that to the Doctor.

Doctor, let me quote from Exhibit 19 from the American Journal. "Most of the CTR-funded grant supports biomedical research not related to health consequences of smoking. In a recent survey of principal investigators funded by the CTR grants in 1989 almost 80 percent of the respondents indicated that none of their research, current or past, examined the health effects of smoking.

"Furthermore, the vast majority of industry-supported research that addressed the health affects of smoking produced findings consistent with the Surgeon General's conclusion that smoking is a major cause of numerous diseases."

Are you aware of those findings, Dr. Glenn?

Mr. GLENN. I am aware of Dr. Warner's article.

Mr. SYNAR. Do you agree with the central conclusion?

Mr. GLENN. What is his conclusion?

Mr. WAXMAN. The conclusion that the CTR research is not related to the health consequences of smoking.

Mr. GLENN. What was the——

Mr. SYNAR. That is what the statement is, that the CTR research is, quote, "not related to the health consequences of smoking." Do you agree with that?

Mr. GLENN. No, sir.

Mr. BLILEY. Can these documents be made available to the members? We don't have them.

Mr. WAXMAN. We will get them to you immediately.

Mr. SYNAR. Do you know Dr. Brennan? Is he not a member of your Scientific Advisory Board?

Mr. GLENN. Yes.

Mr. SYNAR. In an article, "Pack of Lies", a BBC documentary, Dr. Brennan is quoted as saying that during his service on the Scientific Advisory Board, "very little of the CTR research is related to determining the relationship of smoking to ill health."

Dr. Brennan goes on to say in this BBC documentary that, "certainly less than 1/10 of the funds awarded are awarded for the scientific study of tobacco-related effects."

Is Dr. Brennan correct?

Mr. GLENN. He is correct in the sense that we—I have spent millions of dollars in the past in supporting studies where experimental animals were exposed directly to tobacco smoke and that sort of thing. It was very unrewarding. As the Surgeon General's report will point out to you, there has never been an instance in which lung cancer was observed in animals exposed to intense tobacco smoke. It was an unrewarding avenue of research and we focus now on molecular and cellular aspects, as I have explained. That is what Dr. Brennan was alluding to.

Mr. SYNAR. So the quote that, certainly less than one-tenth of the funds of the CTR awarded are awarded for specific study of tobacco-related effects; you are saying only 10 percent of the budget has anything to do with tobacco?

Mr. GLENN. When he says specifically related to tobacco products, he is talking about research with nicotine, talking about——

Mr. SYNAR. No, he didn't say specific tobacco-related products, he said tobacco-related effects.

Mr. GLENN. That would include nicotine.

Mr. SYNAR. Are you familiar with your Council report of 1993?

Mr. GLENN. I am.

Mr. SYNAR. Out of the 296 studies in your index, where you funded about $19.5 million in grants; as I see from the index only 10 or about 10 of the projects have anything to do with tobacco. Do you dispute that?

Mr. GLENN. No, sir.

Mr. SYNAR. So you don't devote much research to cigarettes or the death of the 434,000 Americans a year, do you?

Mr. GLENN. Because, Mr. Synar, medical research in general has taken the turn towards basic fundamental understanding of cell regulation and deregulation. Until we understand these processes, we cannot explain any diseases. And our research is at the forefront, along with that of the National Cancer Institute and the National Institutes of Health and the various other private funding agencies.

Mr. SYNAR. Dr. Glenn, has the Council for Tobacco Research conducted or financed research that has found that smoking cigarettes or using oral tobacco increases the likelihood of a person developing lung cancer or heart disease?

Mr. GLENN. I didn't hear your question, sir.

Mr. SYNAR. Has the CTR conducted or financed research that has found that smoking cigarettes or using oral tobacco increases the likelihood of a person getting lung cancer or heart disease?

Mr. GLENN. Yes, sir.

Mr. SYNAR. Will you provide that for the committee?

Mr. GLENN. Yes, sir, it is provided in the annual reports that you already have at hand.

Mr. SYNAR. Dr. Glenn, has the Council for——

Mr. WAXMAN. Just a moment, we want to receive specifically from you an answer, do not just refer us to some other document.

We will hold the record open but we want a specific response to that question.

Mr. SYNAR. You will provide that full report?

Mr. GLENN. Yes, sir.

[The following information was received:]

At the hearing, I was asked about studies funded by the Council that found that tobacco use increased the likelihood of disease. With all due respect, this request is extremely naive, and therefore very difficult to respond to meaningfully. Modern scientific studies into the etiology of chronic diseases typically focus on narrow questions, the answers to which contribute to a broader understanding of disease processes. However, as a general matter, each such study, standing alone, does not state that smoking does or does not make the chronic disease more likely. The reported research findings have implications for the relationship between smoking and disease that are far more subtle, complex and cumulative.

Consequently, in many instances, it is difficult to determine—and it ultimately is a subjective matter—whether a publication is deemed to have found an increased likelihood of disease. Indeed, I believe that any two persons who might review the full set of publications resulting from the Council's grants in response to this request would come up with different sets of documents. As I stated on May 26 in response to this request, abstracts of publications resulting from CTR grants and contracts have appeared in the Council's annual reports, and we can make the publications themselves available to the subcommittee for its review.

With these qualifications, we are providing in the boxes marked "Box 1" and "Box 2" copies of over 375 publications resulting from Council-funded research that could be considered to indicate that tobacco use may increase the likelihood of developing diseases or conditions that have been associated with smoking. (These documents were selected from the Council's files of publications resulting from Council grants. Those files are not complete since not all publications have been provided by the researcher or located in the Council.) We have used our best efforts to compile for the subcommittee a complete set of such publications, in light of the difficulties referred to above. In addition, in order to reduce the burden on the subcommittee, we are not providing copies of publications that simply rely on or refer to previous research findings associating smoking and diseases, and in a number of instances we are not providing copies of publications that are preliminary to, or repetitive of, publications that are being provided.

Mr. SYNAR. Dr. Glenn, has the CTR conducted or financed any research into the matter that nicotine is addictive or has an addictive quality to it?

Mr. GLENN. We have sponsored a very large amount of research into nicotine. We have been very concerned about the question of addiction. We have funded researchers who have established the habituation of nicotine. We have not been able to establish addiction. Indeed, we asked Dr. Jerome Jaffe, Director of the Addiction Center at the National Institute of Drug Abuse to address our Scientific Advisory Board on this question in 1989. Dr. Jaffe and our Scientific Advisory Board had a lengthy exchange.

Dr. Jaffe was unable to assign properties of addiction as they are classically defined to nicotine. We have continued to pursue the question and are doing so now.

Indeed, a large part of this conference that is taking place here in Washington today deals with nicotine and nicotinic receptors. I think the committee should know that the central nervous system, the function of the central nervous system and myoneural junctions depend upon two sorts of chemical receptors. They are classified as muscarinic and nicotinic.

Perhaps the word "nicotinic" is unfortunate but nicotine and nicotine analogs we derive from the various foods that we eat, to say nothing of nicotine that might be in tobacco is critical to normal neural function in the human being.

Mr. SYNAR. Just a couple things on that very one point. Dr. Jaffe is a member of the National Institute on Drug Abuse that did find that nicotine is addictive, is he not?

Mr. GLENN. Dr. Jaffe is—was at the time he appeared before us the Director of the Addiction Center for the National Institute of Drug Abuse.

Mr. SYNAR. All right. Now beyond Dr. Jaffe, let me repeat this question very clearly. Have you conducted or financed research that has found nicotine is addictive or has an addictive quality to it?

Mr. GLENN. We have definitely established that there is habituation to the use of nicotine. We have not established addiction.

Mr. SYNAR. Will you provide for the record all of the reports and studies with respect to nicotine and its addictiveness?

Mr. GLENN. Yes, sir.

Mr. SYNAR. Thank you.

Mr. WAXMAN. Mr. Synar's question was have you financed studies on nicotine and nicotine addiction. You then answered that you have concluded it is habituating. Have you financed studies?

Mr. GLENN. I misspoke, Mr. Waxman. I didn't conclude, the investigators concluded. We funded the projects. Yes, sir, extensive.

Mr. WAXMAN. You will give us details of those studies.

Mr. GLENN. Yes, sir.

Mr. WAXMAN. In fact, the studies themselves?

Mr. GLENN. Yes, sir.

[The following information was received:]

The two boxes of documents marked "Box 3" and "Box 4" contain copies of over 560 publications resulting from Council-funded research that appear to examine the effects of nicotine. (As explained above, the set of publications from which these documents were selected is incomplete.) Again, we have used our best efforts to compile for the subcommittee a complete set of such publications.

As I mentioned during my testimony on May 26, during the week of my testimony the Council sponsored an important seminar on central nervous system receptors, including the receptors that respond to nicotine and its analogues. Item I in the Appendix includes copies of the program from that seminar and of the abstracts presented at that seminar.

Mr. WAXMAN. Mr. Greenwood.

Mr. GREENWOOD. Thank you, Mr. Chairman.

Good morning, Dr. Glenn.

Mr. GLENN. Good morning, Mr. Greenwood.

Mr. GREENWOOD. In all of my questions I am going to be referring to the February 11, 1993, Wall Street Journal article.

The article notes that the Supreme Court last year said smokers can sue, accusing the industry of deliberately hiding or distorting smoking dangers.

Can you inform us as to what the record of those suits has been, the number of such suits filed, and whether your organization been a defendant in those suits?

Mr. GLENN. In the two suits mentioned in this article?

Mr. GREENWOOD. I am asking a more general question. Has your organization been sued as a result of the Supreme Court's ruling that the industry has deliberately been hiding or distorting smoking dangers? Have you been a defendant in such a suit?

Mr. GLENN. The Council for Tobacco Research has been named defendant in a number of tobacco-related actions.

Mr. GREENWOOD. Can you tell us about the status of those cases? Have any drawn to conclusion yet?

Mr. GLENN. There have never been adverse findings against the Council for Tobacco Research. Indeed, in the Cipollone case the court found that activities of the Council for Tobacco Research were essentially irrelevant to the action at issue there. Subsequently Judge Sarokin issued a statement relative to the Haynes case in which we were not named as a defendant citing some 1,500 secret documents of the CTR as reported in the press.

That simply was not true. The 1,500 documents must belong to somebody else because they certainly didn't belong to us.

Mr. WAXMAN. So you are saying in one case the court found for the Institute as the defendant, is that what you said?

Mr. GLENN. Yes, sir.

Mr. WAXMAN. And have there been cases where the courts have found for the plaintiffs?

Mr. GLENN. Not against the Council for Tobacco Research, no, sir.

Mr. GREENWOOD. OK. There has been a lot of questioning about the freedom of the researchers who have been funded by the Institute, freedom to pursue their research as they would be directed scientifically and freedom to publish. Are those assurances contractually guaranteed to the researchers? Do they have contracts with the Institute that say clearly, you are in charge of directing the course of this research and, second, you are entirely free to publish?

Mr. GLENN. There was no contract per se but in the grant award letter every grantee, there is a paragraph to the effect you are encouraged to publish your results. We look forward to receiving reprints of your publications and that message is reiterated to grantees repeatedly.

Mr. GREENWOOD. Have you made those letters available to the committee yet?

Mr. GLENN. I can—I am not sure that we have, Mr. Greenwood. I would be happy to provide them.

Mr. GREENWOOD. If you would give us a sample of those.

[The following information was received:]

Item D in the Appendix is a copy of a form letter, with attachments, that is provided by the Council to successful grant applicants. One of these attachments, "Important Procedural Information for Grantees", refers specifically to publications by grantees. Item E in the Appendix is the Council's Statement of Policy, which is sent to all grant applicants. The Statement of Policy makes it clear that the Council expects grantees to report their findings in medical and scientific journals, and requests that any publications acknowledge the Council's support.

Our Statement of Policy also says, in very clear terms: "The Council desires to have scientists work with the greatest freedom, without domination of any kind. It will make no attempt to direct the administration of a project once started, to influence its course or to control its results . . ." That is the Council's fundamental policy: to give complete scientific freedom to its grantees, and to let the chips fall where they may.

Mr. GREENWOOD. The question of the independence of the researchers that receive your grants further comes into question in the Wall Street Journal article. I will quote, "for both men defying conventional wisdom has been rewarding; Dr. Seltser says he has received well over $1 million from the Council, Dr. Sterling got $1.1 million for his special projects works, the 1977 to 1982 court records show."

Can you inform this committee how the level of the grants compares with normal practice? Were your grants particularly high? Was there any attempt by the Institute to make sure that scientists were not so well paid for their research that they felt they would be inclined to feel that they couldn't receive grants as lucrative elsewhere?

Mr. GLENN. Most of our grants are much smaller in nature. The average grant from the Council for Tobacco Research is of the magnitude of $75,000 to $80,000 per year for 3 years.

However, there are projects that are deemed of such importance that we have given prolonged funding to them. The classic example of this is the research done by Dr. Lynch in the epithelium cancers. We have supported Dr. Lynch for many years because the NIH did not see fit to do so. It is now proving to be a gold mine of basic information about genetic disorders and their relation to disease.

So, yes, some of the grants have run to very large numbers simply because of the protracted nature of support.

Mr. GREENWOOD. When you provide a grant to a university or to a research laboratory, does the Institute control the amount of grant that can be taken by the individual researchers for their salaries?

Mr. GLENN. Yes, sir. We do. We regard—in general, the salary of the investigator is to be a responsibility of the institution. We try in as many instances as possible to limit financial support to support personnel such as lab technicians, to the purchase of supplies, experimental animals, publication costs, so forth.

So it is unusual for an investigator to receive any or even a significant part of their salary from the grant.

Mr. GREENWOOD. OK.

Another quote from the Wall Street Journal article, "Today Dr. Hamburger adds that Mr. Jacob—and I assume Jacob is from the law firm—told him he would never get a penny more if the paper was published without making the changes."

This went to the issue of a study that was done by Dr. Hamburger years later at the Rose Cipollone tobacco liability trial in Federal Court in New Jersey. The issue is whether the researchers could use the term "cancer." Apparently the allegation in the article is that the law firm representing the Institute did not want the researchers to use the term "cancer", they wanted them to use more obscure medical terminology. Dr. Hamburger allegedly resisted that and claims he was told by Mr. Jacob that his refusal would end his funding. What is your response to that allegation?

Mr. GLENN. First of all, I didn't know Dr. Hamburger and I didn't know Mr. Jacob. But I do know the circumstances.

Dr. Hamburger was a grantee of the Council for Tobacco Research. He was working on the induction of lung tumors in animals. His work was very nonproductive.

He was able to produce only a superficial change in the epithelium of the lung, never any tumors. As a consequence, the Scientific Advisory Board declined to extend his funding. He was funded I think for some 6 years. But the work was nonproductive and they did not renew his grant.

I think his statements may reflect some bitterness at the fact that his funding was not continued. He was not successful in getting funding from any other agency.

Mr. GREENWOOD. How do you respond to that part of his allegation that says that he was asked not to use the term "cancer" in his research but to use——

Mr. GLENN. Because our Scientific Advisory Board could not confirm that he had induced cancer; only superficial changes.

Mr. GREENWOOD. Another quote from the article, "By 1968 the Council had begun putting researchers under contract for many studies. This gave it the right to control both the studies design and publication of the results."

I believe in response to an earlier question that I asked, you indicated that there were not contracts, they were in fact grant letters. There seems to be an inconsistency.

Mr. GLENN. No. Contract research was done. It was not a prominent part of the activity of the Council for Tobacco Research. As

I am informed, there were some contract studies in years past. There are none today.

In years past, there was a major contract with microbiological associates, and some several million dollars were spent in exposing laboratory animals directly to tobacco smoke in an effort to produce tumors. It was an unsuccessful effort. It went on for a number of years and finally the Scientific Advisory Board, which had oversight over this contract research, decided that it was inappropriate to continue with the research and the contract was terminated. It ran through its end. It simply was not renewed.

Mr. GREENWOOD. Did that contract contain within it terms specifying the relative amount of freedom of the researchers to direct the research or their freedom to publish?

Mr. GLENN. Yes, sir, as a matter of fact a major publication resulted from that Micro-Biological Associate's research work.

Mr. GREENWOOD. So the contract did specify that the researchers were in control of the direction of the research and were free to publish their findings as opposed to the contract specifying that the Council would determine the course of their science and whether or not they could publish, is that correct?

Mr. GLENN. Yes, sir. To my knowledge there never was no restriction. I think a number of publications by Micro-Biological Associates resulted from that work.

Mr. GREENWOOD. Could you make a copy of that contract available to this committee?

Mr. GLENN. Yes, sir.

[The following information was received:]

Item G in the Appendix includes copies of each of the Council's contracts with Microbiological Associates, Inc. ("MAI"), together with contract renewals. The Council spent some $12 million under the MAI contracts on a large-scale, long-term study of the effects of smoking inhalation on mice.

I was mistaken when I told the subcommittee that these contracts contained no restriction on publication by MAI. The Council has had no research contracts during my tenure, and I had erroneously assumed that the Council's policies with respect to publication by contract researchers were the same as its policies with respect to publication by grantees. Since my testimony, I have learned that the MAI contracts provided that the Council's prior written approval was required for MAI to publish its research findings. Such provisions are customary in research contracts.

It is my understanding that the results of the major inhalation study performed by MAI were published in complete and unedited form. In addition, MAI published dozens of articles based on its Council-funded research. Item H in the Appendix is a list of 89 publications or abstracts that appear to have resulted from the Council's support of MAI, at least 73 of which acknowledge support from the Council.

Mr. GREENWOOD. Finally, Mr. Chairman. Another quote from the article: "But lawyers from Jacob Mettinger told Micro-Biological the project would go no further. When a contract is canceled given these kinds of results, Dr. Henry says, reasonable scientists might conclude the liability issue must have suddenly become apparent to this group."

You already disputed the use of the terminology contract being canceled, you said it simply was not renewed. Was it in fact the case that the decisions about whether such a contract would be continued was made by lawyers from Jacob Mettinger or was that decision made by the Council?

Mr. GLENN. To my knowledge—again, Mr. Greenwood, I was not there—but to my knowledge what I have been told, Scientific Advi-

sory Board determined that they had spent several million dollars, it was nonproductive, and they could put the funds to better use in other activities.

Mr. GREENWOOD. So it is your testimony that the lawyers from Jacob Mettinger simply were the conveyers of information from the Council to the researchers, that they did not participate in the decision-making mode as to whether the contract would be continued or how the course of the research would go?

Mr. GLENN. I have no direct knowledge of that. I believe that to be the case.

Mr. GREENWOOD. Thank you, Mr. Chairman.

Mr. WAXMAN. Thank you, Mr. Greenwood.

Mr. Wyden.

Mr. WYDEN. Thank you, Mr. Chairman.

Mr. Glenn, do you know a gentleman named Mr. Addison Yeaman?

Mr. GLENN. No, sir, I don't know him.

Mr. WYDEN. You have no knowledge of him?

Mr. GLENN. I know of him. I do not know him.

Mr. WYDEN. I thought since you lived in Kentucky and I understand he spends a fair amount of time in Kentucky also, that you may have spoken several times over the years?

Mr. GLENN. No, sir. I have never met Mr. Yeaman, I have never talked to him.

Mr. WYDEN. OK.

Do you know a woman by the name of Dorothea Cohen?

Mr. GLENN. I don't know her, Mr. Wyden. She was terminated as a librarian at the Council about the time I joined the Scientific Advisory Board.

Mr. WYDEN. So you have no recollection of any discussions with her on various tobacco issues over the years?

Mr. GLENN. No, I have never discussed it with her. I am sure the committee knows Ms. Cohen is very ill.

Mr. WYDEN. That is not what I asked you. I wanted to know about two individuals and whether or not you had any discussions with them. The first was Mr. Addison Yeaman. You have told us under oath that you do not know Mr. Yeaman nor have you had any discussions with him. Is that correct?

Mr. GLENN. That is correct.

Mr. WYDEN. And the same is true for Ms. Cohen?

Mr. GLENN. That is correct.

Mr. WYDEN. Thank you.

Could you cite a particular research report funded by your organization which argues there is a causal relationship between tobacco use and lung cancer?

Mr. GLENN. Mr. Wyden, I cannot because I cannot accept the causal relationship. Causal relationship in medicine and science is a 1-1 proposition. If one were to encounter the tuber bacillus and they get tuberculosis, that is cause and effect. The industry and the Council for Tobacco Research freely acknowledge the risk factor of smoking. Nobody denies that. We certainly recognize it.

The vast bulk of our research has been directed towards some disposition of that particular problem. We cannot accept the term "cause" in a scientific sense.

Mr. WYDEN. I ask because one would think that as an allegedly objective organization, you might possibly have funded just one paper that argued the kind of causal relationship that virtually every unbiased medical organization in our country argues exists.

You have told us you have not funded one, and we accept your word.

Mr. GLENN. Mr. Wyden, I reject the premise that we are a biased—I reject the premise that we are a biased organization. I reject the premise that smoking causes cancer. I reject the inference that the purpose of our activities has been to obscure the truth. On the contrary, they have been dedicated to developing scientific truth.

Mr. WYDEN. Well, is it true that you do not agree with all of these organizations?

Mr. GLENN. No, sir.

Mr. WYDEN. The Surgeon General, the American Medical Association, and the World Health Organization have all talked about the causal link between tobacco use and these illnesses. Let me ask you another way since you cannot cite us any report that addresses this causal link.

What percentage of your recent research has even looked at the causal links between smoking and cardiovascular problems, emphysema, and cancer?

Mr. GLENN. If you accept cause in the lay sense, I would say all of it. If you use the term "cause" in the scientific sense, I would say none of it.

We are looking for the underlying problems that predispose individuals. For example——

Mr. WYDEN. You just said that if you look at it in a scientific sense—these are your words, not mine—and your organization is a scientific organization, you have not done any research to examine these causal links.

Mr. GLENN. Mr. Wyden, obviously I didn't make my point and I apologize for that.

Mr. WYDEN. Please feel free to elaborate. This is an opportunity for you to set the record straight.

Mr. GLENN. No one has been able to demonstrate that smoking per se causes any diseases. It is clear that it is a risk factor, and we all knowledge that. Nobody can live in this world today without recognizing that smoking is a risk factor for lung diseases, cardiovascular diseases, perhaps for many things we don't even know about yet.

On the other hand, what we have got to find out is why the cell goes wrong. If it is exposed to this environmental agent, tobacco smoke, what makes the cell go wrong? We know, for example, that 93 percent of smokers smoke for years never developed any lung disease, 7 percent do.

Why is there that vast discrepancy? Why do some people escape this injury completely? That really is what we address our research to.

Mr. WYDEN. Do you believe that smoking causes cancer?

Mr. GLENN. No, sir.

Mr. WYDEN. Do you believe smoking is addictive?

Mr. GLENN. No, sir.

Mr. WYDEN. Do you realize your opinion stands alone in comparison with all of these major medical groups that I have cited?

We are talking about isolation. We are not talking about some sort of——

Mr. GLENN. Mr. Wyden, I am not isolated as a scientist. If you asked scientists to give you a scientific opinion about cause and effect, you will find that I am in the vast majority. The risk factors of smoking are well-known. Nobody is arguing about that.

What I am trying to impress on you is that there are much more fundamental issues here in the matter of predisposition to various disease processes that must be elaborated before we can address other fundamental issues.

As to the matter of——

Mr. WYDEN. I don't know how an issue gets more fundamental than looking at questions of cause, effect, and addiction. You told me from a scientific standpoint that you don't even look at any possible connection between smoking and disease, and I think that is an extraordinary statement for an organization like yours to make. This leads me to the additional area I want to explore, which is, in my view, that you are a public relations shop essentially posing as the National Cancer Institute.

You have said to my colleagues again and again that you are doing all this scientific work. You just told me that you have not done any recent studies to look at the causal links between smoking and disease, and I would like to now ask you what kinds of activities you perform in a public relations sense. Certainly Ms. Cohen told the Wall Street Journal that you were a public relations shop and a lobbying shop. I quote her, "The Council for Tobacco Research is just a lobbying thing. We were lobbying for cigarettes."

Do you perform public relations functions or lobbying functions?

Mr. GLENN. Mr. Wyden, I won't respond to your editorial but I will respond in the matter of Ms. Cohen. Ms. Cohen has multiple sclerosis. It is an established medical fact that people with this severe debilitating neurologic disease develop mental problems as well.

Since making that statement to the press, Ms. Cohen has called our office and tearfully apologized for her statements. I am very sorry for the lady and I really don't think her name ought to be invoked in this Congressional subcommittee.

Mr. WYDEN. In your opinion, at the time that she made these statements to the Wall Street Journal, she was not capable of being objective or truthful?

Mr. GLENN. That was her statement to our staff member.

Mr. WYDEN. All right. Could you get us anything that would document that? I have not seen anything that would suggest that she repudiated it at any time when she was capable of doing so.

[The following information was received:]

At the May 26 hearing, I was asked to supply documentation for my statements about Dorothea B. Cohen, the former Council employee to whom comments were attributed in the Wall Street Journal article of February 11, 1993. We had intended to respond to the subcommittee's request for documentation by obtaining an affidavit from Ms. Cohen, setting forth her view that the Wall Street Journal article was inaccurate. However, Ms. Cohen has moved, and we have been unable to locate her. We have spoken with Dr. John E. Bevilacqua, Ms. Cohen's treating neurologist (who is also her cousin.)

Dr. Bevilacqua has provided us with a letter dated August 20, 1994, describing Ms. Cohen's medical condition as of that date and as of February 11, 1993, when the Wall Street Journal article appeared. Dr. Bevilacqua has asked that his letter be treated as confidential, in deference to Ms. Cohen's privacy interests. We expect to provide Dr. Bevilacqua's letter to the subcommittee promptly after we have reached an understanding with the subcommittee staff with respect to procedures for the subcommittee's handling of materials provided by the Council. In the interim, I respectfully request that my letter be included at page 78 of the May 26 transcript.

I have learned that I was mistaken when I testified on May 26 that, following the publication of the Wall Street Journal article, Ms. Cohen called the Council and apologized to one of our employees for the statements attributed to her in the article. What happened was that shortly after the Wall Street Journal article was published, Ms. Cohen was contacted on our behalf and said that she had been misquoted in the article. The fact that Ms. Cohen had stated that she had been misquoted in the article was reported to an officer of the Council, who in turn reported that to me. As a result, I formed the mistaken impression that Ms. Cohen had called the Council, but my basic understanding about what she did say was correct.

Mr. WYDEN. Let me ask you about one other area, Mr. Glenn. Have lawyers from any of the tobacco companies that fund your research ever attempted to exert influence on research in progress?

Mr. GLENN. No, sir.

Mr. WYDEN. Mr. Chairman, I yield back.

Mr. WAXMAN. Thank you, Mr. Wyden.

Dr. Glenn, you gave a very precise scientific answer to Mr. Wyden's question about the link between cigarette smoking and all these diseases like cancer, emphysema, and heart problems.

But if I asked you as a scientist in an independent organization for your recommendation to me as an adult whether I ought to smoke or not, if I am concerned about those diseases, do you advise me to smoke or not?

Mr. GLENN. Mr. Waxman, you know, I have been asked that question by many patients who suffer from diseases that are known to have smoking as a risk factor and I would tell you what I have told all of them. For example, a patient with a bladder cancer. There is the implication that by-products of smoking may aggravate bladder cancer. I tell those patients spontaneously without them asking that I think they ought to stop smoking since it is a risk factor.

Mr. WAXMAN. If I was asking for general health advice, do you think that people ought to smoke or not?

Mr. GLENN. I think people ought to have free choice. It is a legal product as is alcohol and other substances. I think they should have the information and I think that the information is readily available both in the scientific community and the lay community.

Mr. WAXMAN. I am not asking you for what public policy ought to be and whether people ought to be permitted to smoke.

I am asking you from you as a scientist and health expert what your recommendations are. Do you think people ought to smoke?

Mr. GLENN. I think that is a very simplistic, Mr. Waxman. Do I think people ought to drive automobiles at 140 miles an hour on the interstate? Clearly there are risk factors involved in everything we do every day. I think every patient should——

Mr. WAXMAN. I assume, then, you would tell people that they shouldn't smoke at 140 miles an hour?

If you are willing to tell them that about speeding, would you also be willing to tell them that you think that they ought not to

smoke because it is taking an inordinate risk, that they may well get cancer, heart disease, emphysema, and bladder cancer, and all these other problems?

Mr. GLENN. I come back to what I have said before, 93 percent of people who smoke never develop lung problems. On the other hand, I know perfectly well, and I tell patients, 80 percent of the people who die of lung cancer have been smokers. The interesting aspect is that 20 percent of people who die of lung cancer have never smoked.

Mr. WAXMAN. Dr. Glenn, I suspect that you have strong views of your current mission of CTR. Can you share with us what you see that mission to be?

Mr. GLENN. I see our mission to be one of elaborating fundamental mechanisms of diseases and we have found that the specific research into exposing animals to cigarette smoke is superficial and nonproductive.

Mr. WAXMAN. My staff is telling me that since we are starting a second round of questions, if you want to take a break we can take a short break now.

Mr. GLENN. I am perfectly happy, thank you, sir.

Mr. WAXMAN. OK. Could you help us in understanding how CTR is funded? I believe the original budget in 1954 was $1 million. Is that correct? Do you know?

Mr. GLENN. I believe it is, Mr. Waxman. I forget.

Mr. WAXMAN. The current budget is $19 million.

Mr. GLENN. Nineteen million five hundred fifty thousand dollars.

Mr. WAXMAN. Where does the money come from?

Mr. GLENN. Comes from the five major sponsor companies.

Mr. WAXMAN. From 1994, what was the method of apportionment of funding among your member companies and what are the actual dollar amounts?

Mr. GLENN. I can't tell you the actual dollar amounts from each company, but roughly the contributions of the companies are based upon their market share, a formula that they derived years ago.

Mr. WAXMAN. Would you give us for the record that information, and all past budgets and the share each company paid for each year of your organizations existence?

Mr. GLENN. I am sure we can develop that.

[The following information was received:]

We have prepared three separate tables setting forth the dollar amounts contributed in each year, by each contributor, to the Council and to the Tobacco Industry Research Committee ("TIRC") for the General Fund, for Council Special Projects, and for the Council's Literature Retrieval Division ("LRD"). (I understand that LRD was a division of the Council from 1971 until 1983, that LRD compiled medical literature for the use of the tobacco companies, and that LRD's assets were transferred in 1983 to LS, Inc., a corporation that is unrelated to the Council.) This financial information is non-public, and the Council's members regard it as confidential. We expect to provide these tables to the subcommittee promptly after we have reached an understanding with the subcommittee staff with respect to procedures for the subcommittee's handling of materials provided by the Council. In the interim, I respectfully request that this letter be included at page 82 of the May 26 transcript.

We have collected copies of the audited financial statements of the Council and its predecessor for each year from 1963 through 1993. (In 1983, the Council changed from a calendar year to a November 1 fiscal year.) We have also collected copies of budgets for each year from 1954 through 1962; we are unable to locate financial statements from before 1963. Again, this financial information is non-public, and

the Council and its members regard it as confidential. We expect to provide these tables to you promptly after we have reached an understanding with the subcommittee staff with respect to procedures for the subcommittee's handling of materials provided by the Council. In the interim, I respectfully request that this letter be included at page 82 of the May 26 transcript.

Item F in the Appendix is a copy of the Council's current by-laws. Article III of the by-laws provides the method of apportioning the funding of the Council among its sponsors.

Mr. WAXMAN. What is the tax status of the CTR?

Mr. GLENN. We are a not-for-profit organization.

Mr. WAXMAN. With regard to your organizational structure—you are in charge of the organization, is that correct?

Mr. GLENN. That is correct.

Mr. WAXMAN. Can you tell the subcommittee what the Committee of Councils is?

Mr. GLENN. What the Committee of the Council is?

Mr. WAXMAN. Or Councils.

Mr. GLENN. I am not sure I understand the question.

Mr. WAXMAN. Well, I have heard there is a Committee of Councils. I want to know does it function within CTR or is it an independent organization?

Mr. GLENN. Mr. Waxman, I don't recognize the term at all.

Mr. WAXMAN. You don't know what that is?

Mr. GLENN. I will be glad to explain our organizational structure, but I don't understand that question.

Mr. WAXMAN. OK. Can you make research funding decisions without first obtaining specific approval from anyone else?

Mr. GLENN. Yes, sir.

Mr. WAXMAN. Have you ever done this or are you aware of any instances where the chairman has done this?

Mr. GLENN. Where the chairman has made the decision?

Mr. WAXMAN. Right.

Mr. GLENN. I am sure you understand that our Scientific Advisory Board really is the decision-making board and it functions much like a study section of Federal Government organizations. Almost identical.

Mr. WAXMAN. Is that also known as the Scientific Liaison Committee?

Mr. GLENN. I don't know that term, Mr. Waxman.

Mr. WAXMAN. OK. So you have never heard of a Scientific Liaison Committee, but there is a Scientific Advisory Board, is that correct?

Mr. GLENN. Yes, sir. Maybe it would simplify things, Mr. Waxman, if I were to tell you that the Council for Tobacco Research, of which I am president, chairman and CEO, consists of 15 individuals, 5 of them hold PhD's or equivalent degrees in basic medical sciences; the remainder of the staff are largely clerical in their activities.

Mr. WAXMAN. Let me ask you on a different topic, do grantees and contractors get paid directly by CTR or is payment made by individual tobacco companies?

Mr. GLENN. Grantees of the Council for Tobacco Research are not reimbursed directly. The institutions that they represent become the grantee and they, the institutions, are responsible for distribution of these funds. That process is identical to that of the NIH.

Mr. WAXMAN. The institutions, you mean the universities or——

Mr. GLENN. The universities, or the research institute.

Mr. WAXMAN. Are those institutions paid by CTR or are they paid by the individual tobacco companies?

Mr. GLENN. By CTR.

Mr. WAXMAN. And how many people work for or are under contract to CTR at the present time?

Mr. GLENN. Under contract?

Mr. WAXMAN. Yes.

Mr. GLENN. We have no contracts at the present time. We have independent research grants but no contract research at the present time.

Mr. WAXMAN. How many of your employees are legal staff?

Mr. GLENN. None.

Mr. WAXMAN. How many, not counting the Scientific Advisory Board, are physicians and scientists?

Mr. GLENN. Not counting the Scientific Advisory Board, six including myself.

Mr. WAXMAN. And will you provide for the record the past and present personnel roster with divisions by areas of job responsibility for each year from 1954 to the present time?

Mr. GLENN. Yes, sir.

[The following information was received:]

We have prepared a list setting forth the names, years of employment and the current (or terminal) position of employees of the Council and TIRC from 1954 to the present. I should advise you that while our staff expended considerable time and effort in trying to compile a list of all Council employees, the list may not be complete or totally accurate because the Council's records for this 40-year period are incomplete.

In deference to the privacy interests of the persons whose names appear on this list, we regard it as confidential. We expect to provide this list to the subcommittee promptly after we have reached an understanding with the subcommittee staff with respect to procedures for the subcommittee's handling of materials provided by the Council. In the interim, I respectfully request that this letter be included in the May 26 transcript.

Mr. WAXMAN. In 1993, what percentage of CTR research and what percentage of CTR research funds involves projects directly relevant to the health hazards of smoking and can you provide information for us for each past year?

Mr. GLENN. Well, our mission, Mr. Waxman, is to investigate the areas relating to tobacco and health and all of our research can be said to be relevant to that issue.

Mr. WAXMAN. And how much is directly related to health hazards of smoking?

Mr. GLENN. Again, Mr. Waxman, I am repeating what Mr. Wyden asked me and that is that all of the research can be related to issues of tobacco and health.

Mr. WAXMAN. Mr. Bliley asked you for a submission for the record of publications from presentations resulting from CTR's special projects, and Mr. Greenwood I think made some similar requests.

You said in response to Mr. Greenwood you were not holding any special projects documents. Would you give us all documents in your possession relating to special projects, including grant applications, grant reviews, all correspondence with the recipients of these grants?

Mr. GLENN. Mr. Waxman, the special projects were not submitted as a regular grant. Therefore, we have no grant application. These were projects that were deemed worthy of pursuit by our sponsor companies. We were asked to be the administrative servicing agent only. So we don't have grant applications in the true sense. We know the nature of the project but they do not go through the regular granting process and they do not impact upon our research budget. As I further said, there are no special projects at the present time either.

Mr. WAXMAN. I would like to draw your attention to Exhibit 18, if staff would make that available to you.

This exhibit is a series of letters written from scientists to tobacco industry lawyers, including the firm of Shook, Hardy & Bacon seeking research grants. For instance, the first letter is from Dr. Eleanor MacDonald. She is submitting a budget to enable her to complete work on environmental factors that cause death, dated June 27, 1977, and she seeks $88,773 to complete the work.

Did the Council fund these projects after the lawyers approved them?

Mr. GLENN. Mr. Waxman, this was in 1977 and that precedes my time. These are not records from our files so this is entirely new to me. I really can't comment authoritatively about it. It appears to me to be a letter from an investigator who was accomplishing a special project but that is really all I can tell you.

Mr. WAXMAN. We have Exhibit 16 which is the list of CTR special projects.

Let's be sure that you have that exhibit.

The first page exhibits that Dr. Eleanor MacDonald received a grant of $88,773 in August 1977 from the CTR special projects, 2 months after she wrote the lawyers at Shook, Hardy & Bacon. One would think either this is a coincidence or demonstrates that lawyers were actually reviewing and approving CTR special projects. What do you think?

Mr. GLENN. It would not surprise me at all. Attorneys are called upon as expert witnesses and expert investigators all the time. I have been called many times as an expert witness in medical malpractice actions, and it doesn't surprise me that the attorneys might have recommended a contract with an investigator.

Mr. WAXMAN. Why wouldn't the Science Advisory Committee be reviewing this? Why would lawyers be reviewing it?

Mr. GLENN. Because it is outside the purview of the Scientific Advisory Board. I don't know the nature of the project. I have not seen this document until this moment.

Mr. WAXMAN. Of course this is CTR money that is being used to fund the special project.

Mr. GLENN. It is industry money, Mr. Waxman, and we merely acted as the administrative agent in funding the research.

The companies and the attorneys I am sure do not have any particular expertise in dealing with university finance offices which are unique.

Mr. WAXMAN. Why wouldn't the tobacco companies do this on their own? Why would they use you as an intermediary? Why would they engage in this device?

Mr. GLENN. I don't know why they chose to do that, Mr. Waxman.

Mr. WAXMAN. Why would CTR want to cooperate?

Let me read to you from the Los Angeles Times of today; in 1978 memos to top B&W executives—they were told that CTR solved a huge legal quandary involving the industries' need to both fund research and be able to dismiss adverse findings, and they are avoiding this research dilemma to a responsible manufacturer of cigarettes which on the one hand needs to know the state of the art and on the other hand cannot afford the risk of having in-house work turn sour.

The point here is the value of having CTR doing work in a nondirected and independent fashion as contracted work either in-house or under B&W contract which if it goes wrong can become the smoking pistol in a lawsuit.

So this seems to indicate that the companies used you or your organization as a way to have a deniability for that research which could come back to haunt them in lawsuits. Is that an accurate statement?

Mr. GLENN. I don't think so. The nuances escape me a little bit. But let me put it to you this way. Any time the CTR served as the administrative agent for special projects, we informed the recipient of those funds that should they publish they should acknowledge that this was a special project funded through the Council for Tobacco Research.

That tag line appeared on their publications so it was different from a research grant. This was—this was essentially contract work and we served as the funding agent only.

Mr. WAXMAN. Why wouldn't they acknowledge on their document that the company actually funded them?

Mr. GLENN. In many instances as I understand it—this is before my time—several of the companies might have joined in funding a specific project. We were the funding agency.

Mr. WAXMAN. What I read to you from the LA Times was a memo from the general counsel of Brown & Williamson explaining that this is what they were doing, they are trying to get by this legal quandary.

Mr. GLENN. I can't respond to that. I have just seen the memorandum—the article.

Mr. WAXMAN. Why don't you look it over. We are going to have to take a break, you may have heard the bells ring, to respond to a vote on the House Floor. We will do that and return as quickly as possible to continue our inquiries.

[Brief recess].

Mr. SYNAR [presiding]. Doctor, if you could join us at the table again, please.

The Chair recognizes the gentleman from Virginia for questions.

Mr. BLILEY. Thank you.

Dr. Glenn, why did the companies not conduct special project research in-house, do you know?

Mr. GLENN. No, sir, I don't know.

Mr. SYNAR. Hit your microphone, Doctor, so we can hear you.

Mr. GLENN. No, sir, I don't know.

Mr. BLILEY. Dr. Glenn, I am not a scientist but I was intrigued by your testimony about the current focus of CTR research at the molecular level in your belief that the keys to unlocking the mysteries of chronic diseases is to be found by this research. Would you tell us some more about how your views compare with those of other scientists?

Mr. GLENN. I think my views are consistent and consonant with the views of other scientists.

One of the most significant things being done in medical science today is the human genome project to which our government has devoted a great deal of money and effort. In essence, once the human genome is decoded we will be able to identify the genetic—genetically normal patterns and the deviations from the normal patterns that predisposes us to a lot of diseases. A theoretical possibility is that we could identify people who are subject to some disease in the future, and we could either genetically alter their gene's chromosomes or we could advise them about avoiding the risk factors that might predispose them. It is a very exciting thing.

Perhaps by the turn of the century we may have some very positive answers in this area.

Mr. BLILEY. Dr. Glenn, has CTR-funded research produced results which indicate connections or possible connections between smoking and disease?

Mr. GLENN. Yes, sir.

Mr. BLILEY. During your tenure, has CTR had a public relations function?

Mr. GLENN. No, sir.

Mr. BLILEY. Don't other funding organizations have PR functions?

Mr. GLENN. Well, to the extent that they engage in fund-raising activities, we don't do that because we are funded by the industry. The American Cancer Society, the American Heart Association, do indeed have extensive public relations efforts, and it is entirely appropriate that they do that, because they are raising money from the general public in order to engage in research projects.

Mr. BLILEY. I noted, Dr. Glenn, in my opening remarks, my concerns both about the misapprehension that can result from quoting excerpts from documents out of context and the difficulty of accurately developing the facts before this committee since we were not provided until the last minute with the documents that will be shown to witnesses.

In a very short time I have had to review the Majority staff report and its attachments. I note other documents not mentioned by other members of this committee that should be brought to the public's attention. In particular, I am going to read from Exhibit 8, which is a Hill and Knowlton memo dated July 31, 1954. It seems to me pretty clear that from the beginning CTR was to be involved in relevant research into tobacco issues and health. And I will now begin to read.

"In mid-December, 1953, executives of leading tobacco companies decided some kind of joint action was imperative in the face of widely publicized attacks alleging a link between cigarette smoking and lung cancer. Representatives of Hill and Knowlton, Inc., were

invited to meet with these executives for consultation on ways and means of dealing with the problem.

"At this first meeting, it was agreed that the wisest course of action would be for the industry to find out through objective research what truth there was, if any, in the charges being made against it. Mr. Hill stated it would be a serious public relations mistake for the industry to make any move that could cause it to be accused of disregard of people's health and under no circumstances could the industry afford to engage in direct controversy with its detractors. With the acceptance of these principles, Hill and Knowlton, Inc. was asked to recommend a program to implement them.

"After 2 weeks of intensive study of the problem, public relations counsel developed a step-by-step program which was discussed at a meeting with a small group of public relations representatives of a number of tobacco companies. Valuable suggestions were made at this meeting and the program was put into final shape and submitted to the principals at another meeting the last week in December.

"Taking into consideration court ruling inhibiting the industry from ordinary trade association activities, the program recommended:

"One, formation of an industry group to be known as the Tobacco Industry Research Committee, dedicated to sponsoring and financing research into all phases of tobacco use and health.

"Two, establishment of a Scientific Advisory Board, to be composed of distinguished research scientists and educators, and a scientific director to guide the research objectives.

"Three, undertaking of continuous editorial research into relevant scientific, statistical, and medical material, past and current, for an effective information program.

"Four, keeping the public informed regarding the committee's activities. As a first step, the newspaper advertisement outlining the industry's plans was proposed, copy for which was submitted.

"The program and the public statement advertisement were approved. The agreed-upon approach was to sponsor genuinely objective research and to bring to public attention the fact that there is now no conclusive proof that cigarette smoking is a cause of lung cancer and other serious problems of human health."

And I thank you, Mr. Chairman.

Mr. WAXMAN. Thank you, Mr. Bliley. Mr. Synar?

Mr. SYNAR. Thank you, Mr. Chairman.

Dr. Glenn, which law firms presently represent CTR, or do you have in-house counsel?

Mr. GLENN. Debevoise and Plimpton.

Mr. SYNAR. So you have outside counsel?

Mr. GLENN. Outside counsel.

Mr. SYNAR. What are the duties of the counsel?

Mr. GLENN. What are the duties of the counsel?

Mr. SYNAR. Did you have inside or outside counsel? Let me ask that general——

Mr. GLENN. We have outside counsel, Debevoise and Plimpton, and their duties are to address any legal issues which effect CTR.

Mr. SYNAR. Do you have in-house counsel?

Mr. GLENN. No, sir.

Mr. SYNAR. OK. Now, do the outside counsels get to see any of the CTR research results before the research results are announced?

Mr. GLENN. No, sir.

Mr. SYNAR. OK. So they see it only afterwards?

Mr. GLENN. If they see it at all.

Mr. SYNAR. OK. In the past has that been the case?

Mr. GLENN. To my knowledge.

Mr. SYNAR. Could it be, could it be that they have been able to review it prior to?

Mr. GLENN. Prior to?

Mr. SYNAR. Releasing the results.

Mr. GLENN. I don't know, Mr. Synar, but I would think not.

Mr. SYNAR. Mr. Glenn, your memory is very selective today.

Mr. GLENN. Dr. Glenn, Mr. Synar.

Mr. SYNAR. Dr. Glenn, your memory has been very selective during this hearing. You seem to not remember anything prior to 1987. Will you make available all materials that are central to this hearing prior to 1987 for subcommittee review?

Mr. GLENN. We will cooperate.

Mr. SYNAR. I didn't ask you that. Will you provide all of the materials available in the files of the CTR for this subcommittee?

Mr. GLENN. All of the materials that you request will be provided.

Mr. SYNAR. I am asking you for all of them.

Mr. GLENN. I don't think you want all of them, Mr. Synar.

Mr. SYNAR. I want all of them. Will you provide those for the committee?

Mr. GLENN. We will cooperate fully with the committee. We will provide whatever you require.

[The following information was received:]

At the hearing, Mr. Synar asked me to provide "all materials that are central to this hearing prior to 1987" and "all of the materials available in the [Council's] files." Tr. at p. 98. I responded that the Council would cooperate fully "and would provide whatever you require." Tr. at p. 99. I did not understand Mr. Synar to be asking for every piece of paper in the Council's files. Rather, I thought he was having me confirm that we would be responsive to the subcommittee's requests. Indeed, I have no way of knowing what documents Mr. Synar regards as "central to this hearing." And it certainly would not be feasible for the Council to produce all of its files to the subcommittee. We estimate that those files include over 2.5 million pages, and I respectfully submit that it would serve no purpose to deluge the subcommittee with documents beyond those that the Council has already gathered in response to the subcommittee's broad requests.

I respectfully request that this letter be included in the record.

Mr. SYNAR. The FDA, Dr. Glenn, is currently very interested in the content of tobacco products and its effects on health as you can see from some of the previous hearings that we have had. If the Food and Drug Administration requests any studies that the CTR has conducted or funded for nicotine or any other ingredients contained in tobacco will you freely provide those studies and related documents to the FDA?

Mr. GLENN. Yes, sir.

Mr. SYNAR. Thank you. Do you know a Dr. Leo Abood, who is a member of your board of directors?

Mr. GLENN. Doctor?

Mr. SYNAR. Abood.

Mr. GLENN. Yes, indeed.

Mr. SYNAR. Are you familiar with his work on nicotine analogs?

Mr. GLENN. Yes, sir.

Mr. SYNAR. Why doesn't the CTR sponsor a nicotine analog or even more research based on nicotine since you have this very valuable doctor on board who could evaluate and supervise the research?

Mr. GLENN. I don't understand your question, Mr. Synar.

Mr. SYNAR. You have an expert on staff in this area. Why don't you sponsor or fund research in that area so that he could help you evaluate it?

Mr. GLENN. You are asking me a negative. We have sponsored a great deal of research on nicotine.

Mr. SYNAR. On the nicotine analogs?

Mr. GLENN. And nicotine analogs.

Mr. SYNAR. OK. You have described your background and medical training. Would you discourage your grandchildren from smoking?

Mr. GLENN. I would present them with the facts at an appropriate time, and I recognize that parents and grandparents often don't have any control over the actions of their children. But would I certainly——

Mr. SYNAR. What are those facts, Dr. Glenn, that you would give your grandchildren?

Mr. GLENN. I have told my children and I would tell my grandchildren that smoking is a risk factor for a number of diseases. I would also tell them it is an expensive habit.

Mr. SYNAR. Would you encourage them?

Mr. GLENN. Encourage them what?

Mr. SYNAR. To smoke?

Mr. GLENN. I would encourage them to make an intelligent decision.

Mr. SYNAR. So you would neither encourage nor discourage?

Mr. GLENN. On the contrary. I would tell them the facts; I would encourage them to make an intelligent decision. It is a personal decision. You can't decide for them.

Mr. SYNAR. Would you say that the facts might indicate that they shouldn't smoke?

Mr. GLENN. I would say that if I were presented with the facts about smoking today that I would choose not to smoke. I can't say what my children would do.

Mr. SYNAR. You have some impressive academic and publishing background credentials. You published I think close to 400 articles. Your field is urology, correct?

Mr. GLENN. Correct.

Mr. SYNAR. What was the background of your predecessor?

Mr. GLENN. My predecessor in what?

Mr. SYNAR. As chairman.

Mr. GLENN. As chairman?

Mr. SYNAR. Yes.

Mr. GLENN. Mr. William D. Hobbs was the previous chairman. He was a former officer of R.J. Reynolds Tobacco Company.

Mr. SYNAR. So he was not a medical physician?

Mr. GLENN. No, sir, he was not.

Mr. SYNAR. Could you help me? What does a urologist know about conducting tobacco research?

Mr. GLENN. Mr. Synar, I am a medical administrator. I am also a scientist. I have done bench research. I have done a lot of clinical medicine. There is not much difference between research into urologic problems and research into other problems. The fundamental techniques of biomedical research are fairly universal.

Mr. SYNAR. So that is what qualifies you in the area of tobacco research?

Mr. GLENN. I am qualified to administer a program of research. I don't accomplish research myself in these areas. But I am very qualified to administer a research granting program.

Mr. SYNAR. Thank you, Mr. Chairman.

Mr. WAXMAN. Thank you, Mr. Synar. Mr. Wyden?

Mr. WYDEN. Thank you, Mr. Chairman.

Mr. Glenn, does your——

Mr. GLENN. Dr. Glenn, Mr. Wyden.

Mr. WYDEN. Dr. Glenn.

Mr. WAXMAN. And this is Congressman Wyden, Dr. Glenn.

Mr. WYDEN. Does your operation offer a system for storage of files?

Mr. GLENN. I misunderstood the question, Mr. Wyden.

Mr. WYDEN. I am interested in knowing whether your organization has a system for storing studies, for example, studies done by researchers, your grantees on other researchers. Do you have a system for storing this?

Mr. GLENN. We have a system for storing all of the information relative to the grants that we make, to the reports that the various investigators send us periodically, to papers that are published by those investigators. Extensive file system. We maintain these files for indefinite periods of time. I hope that is responsive to your question.

Mr. WYDEN. It is. You store research, CTR research, and presumably some research done by other scientists as well.

Mr. GLENN. The Council for Tobacco Research doesn't do any research, Congressman Wyden.

Mr. WYDEN. Your grantees do, is that correct?

Mr. GLENN. The grantees do it. And the specifics of their investigations are maintained in their files. What we store are their interim reports to us and any papers that are published, but we do not, for example, maintain a file of their laboratory journals or manuals.

Mr. WYDEN. Who has access to this stored material?

Mr. GLENN. Anyone.

Mr. WYDEN. Anyone?

Mr. GLENN. I——

Mr. WYDEN. The Washington Post, the Wall Street Journal, and the New York Times can come on down and see your storage and information retrieval system?

Mr. GLENN. Well, that would pose a significant burden and I think we would have to ask counsel whether that is appropriate.

Mr. WYDEN. Could this committee come down and see it?

Mr. GLENN. Well, we have agreed to provide you with any information that you want from our files.

Mr. WYDEN. Then access is not in any way limited. This committee, the newspapers and all of the scientific organizations that have interests in this could look at your research files in a consistent, orderly fashion? I am coming down, because I would like to see it. Can I arrange to see what is in your files?

Mr. GLENN. Yes, sir. We would welcome you.

Mr. WYDEN. All right. Mr. Chairman, I yield back. Thank you.

Mr. WAXMAN. Thank you, Mr. Wyden.

Dr. Glenn, this is what we would like from you on the record. We want a list of all of the special projects, a copy of the research results, any correspondence between CTR and the tobacco companies, and/or the researchers regarding any of these special projects. The dollar amount spent on each of the special projects; the itemization of whether and where each special project was published, or if it was published at all; and any other documents in your possession relating to special projects.

Mr. GLENN. Yes, I understand.

Mr. WAXMAN. You will cooperate with us and get those to us?

Mr. GLENN. Yes, sir.

[The following information was received:]

We have gathered 14 boxes of documents, consisting of about 30,000 pages, from the Council's files on Council Special Projects. The vast majority of these documents are from files that are arranged alphabetically by the name of the principal investigator or, in some cases, the investigator's institution. There are also documents from files containing financial information about Council Special Projects and documents from Special Project desk files of certain Council employees. Approximately ⅓ of these pages consist of applications and pre-publication reports by researchers, or evaluations of a researcher or of his or her research. We believe that the information that is reflected in these documents was provided to the Council with a reasonable expectation of confidentiality, and we therefore regard these documents as confidential.

We expect to be able to provide all these documents to you promptly after we have reached an understanding with the subcommittee staff with respect to procedures for the subcommittee's handling of materials provided by the Council. In the interim, I respectfully request that this letter be included in the May 26 transcript.

In addition, I am advised that there are 54 documents from these Council Special Project files that are subject to claims of attorney-client privilege, attorney work-product protection or joint defense privilege asserted by the Council or its sponsors. We do not intend to provide 51 of these documents to the subcommittee, and we intend to redact the other three. None of these documents constitutes a researchers' report of his or her results or findings. (As stated above, the Council has not asserted any privilege with respect to such results or findings; and my understanding is that none of the Council's sponsors have done so.) No communications with scientific researchers are being withheld on privilege or work-product grounds.

[Subcommittee Note: On October 19, 1994, the Council for Tobacco Research submitted to the subcommittee the list of special projects administered by the Council. This list is part of the public record of the hearing and is available for public review in the office of the Committee on Energy and Commerce and the office of Rep. Henry A. Waxman.]

Mr. WAXMAN. Now, in the Haines case Judge Sarokin said he had 1,500 CTR documents in his possession. Will you provide any of these Haines documents that are in your possession, and will you ask the tobacco companies for them and then submit them to us?

Mr. GLENN. Mr. Waxman, you will have to ask the tobacco companies. None of the 1,500 documents to which Judge Sarokin referred were CTR documents. None of them.

Mr. WAXMAN. They were identified as CTR documents.

Mr. GLENN. I am sorry?

Mr. WAXMAN. They were identified as CTR documents.

Mr. GLENN. By the press. I think if you will read the judge's statements, you will find that there is some ambiguity. These were documents apparently referring to CTR, but none of these documents were a part of our files at CTR. None of the 1,500 documents to which he referred are in our files or were ever in our files.

Mr. WAXMAN. Do you know of any reason why a committee of the Congress shouldn't have those documents?

Mr. GLENN. Mr. Waxman, again, that is something that you can deal with the sponsor companies about.

Mr. WAXMAN. My question is, do you know of any reason why they shouldn't be given to us?

Mr. GLENN. I don't even know what the documents are, Mr. Waxman, so I can't respond to that.

Mr. WAXMAN. Then how do you know they are not CTR documents. They are from before your time as chairman.

Mr. GLENN. Mr. Waxman, I assure you, they are not documents from the CTR.

Mr. WAXMAN. And how do you know that?

Mr. GLENN. I know that because we have examined this issue as carefully as possible, and——

Mr. WAXMAN. Who is we?

Mr. GLENN. We internally, the Council for Tobacco Research and its staff in conjunction with counsel.

Mr. WAXMAN. And have you been able to identify these documents?

Mr. GLENN. No, sir.

Mr. WAXMAN. Then how do you have knowledge of these documents if you haven't been able to identify these documents?

Mr. GLENN. I have knowledge of them only from what I read in the paper.

Mr. WAXMAN. You just told me that characterizations by the paper of CTR documents were not accurate.

Mr. GLENN. It is not accurate.

Mr. WAXMAN. And you know that not to be accurate because you reviewed these with your attorneys and perhaps others. Is that correct?

Mr. GLENN. Correct.

Mr. WAXMAN. So how do you know what the documents are or are not?

Mr. GLENN. As I said, Mr. Waxman, we reviewed this internally with our staff and we were further advised by counsel that these were not our documents and were not a part of our files.

Mr. WAXMAN. Then you have not seen the documents?

Mr. GLENN. No, sir.

Mr. WAXMAN. Has your staff seen the documents?

Mr. GLENN. No, sir.

Mr. WAXMAN. Have your lawyers seen the documents?

Mr. GLENN. I can't answer that. I——

Mr. WAXMAN. Then how can you tell us what these documents are or are not?

Mr. GLENN. I have told you——

Mr. WAXMAN. You told me all you know about it is what you read in the newspaper. You said the newspapers, however, have identi-

fied them as CTR documents incorrectly. How do you know it is incorrect?

Mr. GLENN. It is incorrect, I am advised by our own staff and by counsel that these documents were not CTR documents.

Mr. WAXMAN. How do they know?

Mr. GLENN. How does counsel know?

Mr. WAXMAN. How do your staff and your counsel that is advising you know that?

Mr. GLENN. Mr. Waxman, I don't get the thrust of the question. I am simply stating to you a fact, and these are——

Mr. WAXMAN. You have told me they have not looked at the documents. Have they or have they not? If they have not, how can they know whether they are CTR documents or not.

Mr. GLENN. I don't know how counsel can know this, but I accept their reassurance as it stands. They are not our documents.

Mr. WAXMAN. Now, if they are your documents, would you urge that we receive them?

Mr. GLENN. I have no objection one way or the other, Mr. Waxman. They are not our documents. I will be happy to review the documents if you like and tell you whether or not they are CTR documents piece by piece.

Mr. WAXMAN. Well, we would like that and we accept that offer. That would be very helpful.

And will you ask the tobacco companies, or you obviously asked them for them, ask them to receive those documents so you can review them, and then will you submit them to us if they are CTR documents?

Mr. GLENN. No, sir. I think that is your prerogative, but it is not mine.

Mr. WAXMAN. Well, I am asking you to get documents that are CTR documents.

Mr. GLENN. They are not CTR documents, Mr. Waxman.

Mr. WAXMAN. If they are CTR documents after you review them, will you ask the tobacco companies to make them available to us and will you make them available to us?

Mr. GLENN. Mr. Waxman, I don't have the documents. They are not CTR documents. I don't know where this 1,500 CTR documents business came from. But they are not our documents.

Mr. WAXMAN. It comes from the judge in the case. The judge in the case said they had 1,500 CTR documents.

Mr. GLENN. They are documents that perhaps relate to CTR, but they were not in our files. They are not a part of the CTR records. They are not CTR documents.

Mr. WAXMAN. How could they relate to CTR?

Mr. GLENN. I don't know.

Mr. WAXMAN. You just said that you heard that they relate to CTR.

Mr. GLENN. They may carry a message that says Council for Tobacco Research in it somewhere. I don't know.

Mr. WAXMAN. Well, a few minutes ago you told us that your people did a very careful review of these documents and you know that they are not——

Mr. GLENN. No, I did not say we reviewed. I said we did a careful review of our files and I did a careful inquiry of our staff, and I

also submitted the question to counsel, and I am reassured by everyone that none of the alleged documents are from our files. They may relate to CTR, but they are certainly from someone else's files.

Mr. WAXMAN. If they do relate to CTR and you then find that to be the case, will you submit them to this committee?

Mr. GLENN. I don't have the documents, Mr. Waxman.

Mr. WAXMAN. Well, you are going to ask the tobacco companies for the documents.

Mr. GLENN. No, sir, I am not. That is not my prerogative.

Mr. WAXMAN. Then how are you going to review them for us?

Mr. GLENN. I will be glad to if you will submit them to me.

Mr. WAXMAN. Well, I don't want to play games with you.

Mr. GLENN. I am not playing games.

Mr. WAXMAN. You just said a few minutes ago that you will review the documents and if they are CTR documents, you will submit them to us. How are you going to review these documents? I presume you will ask the tobacco companies for them.

Mr. GLENN. I assumed that you would submit them to me. I would be happy——

Mr. WAXMAN. Why would you presume that?

Mr. GLENN. From your statement, Mr. Waxman.

Mr. WAXMAN. My statement was that I was going to submit documents to you? My statement was, will you ask the tobacco companies for these documents.

Mr. GLENN. And I said no, I will not ask the tobacco companies for the documents; I think that is your prerogative. The documents are not my documents, and they are the property of someone else.

Mr. WAXMAN. You don't know whether they are your documents or not.

Mr. Wyden?

Mr. WYDEN. Thank you. If you will just excuse me, I think this is an area maybe we can resolve this way. Do you consider these documents relating to special projects part of CTR files?

Mr. GLENN. I don't know which documents you are talking about, Mr. Wyden. If there are documents in our files relating to special projects, we will be happy to provide them.

Mr. WYDEN. Thank you, Mr. Chairman.

Mr. WAXMAN. Dr. Glenn, do you know whether these 1,500 documents exist?

Mr. GLENN. No, sir, I frankly do not.

Mr. WAXMAN. OK. You indicated to me a few minutes ago you are going to review them one by one and see whether they are CTR documents.

Mr. GLENN. I would be glad to if you would submit them to me.

Mr. WAXMAN. Well, you know, this is a key point. These documents, 1,500 documents, are being kept from the public. I don't know whether they have been kept from you, but they relate to you, they have been described as CTR documents and I think that once they are known to the public, they are going to be pretty damning.

Now I don't see you willing to cooperate with us in getting those documents. Are you willing to ask the tobacco companies to clear your organization? To give Congress the information that the public ought to have, or are we being stonewalled and being told we

are not going to get the documents because you are not willing to help us get those documents presuming you don't already have them and you are just refusing to give them to us?

Mr. GLENN. Mr. Waxman, let me be as plain as I can. The documents are not CTR documents to my knowledge. I do not have access to the so-called 1,500 documents. They are the property of someone else. I don't know whose property they may be. I have not seen the 1,500 documents; I would be happy to review them if you submit them to me and tell you whether or not they relate to internal activities of the CTR. But I think—other than that, I really can shed no light on the issue for you.

Mr. WAXMAN. Well, Dr. Glenn, let me just tell you, I am going to submit some questions to you for the record and we may have to have an additional hearing on this very point.

I want to ask you about special accounts. In preparing for this hearing, we have discovered references to a CTR account called Special Account Number 5. Does this account support scientific research, and who has or had control over this account, and will you provide the subcommittee with a list of the individuals who received funding from this account, the amount of funding, and the purpose of funding?

Mr. GLENN. We will.

Mr. WAXMAN. Can you answer any of those questions now?

Mr. GLENN. I have no idea what Special Account Number 5 is, Mr. Waxman.

Mr. WAXMAN. OK. Well, we believe this was a lawyer-administered special projects fund, but we will get a chance to find out whether that is accurate or not when you submit it to us.

I would like to know what is Special Account Number 4. Does this account support scientific research? Who has or had control over this account? And will you provide the subcommittee with a list of the individuals who received funding from the account, the amount of funding and the purpose of funding?

Mr. GLENN. We will, and we will cooperate with you. Would you identify what special account 4 and 5 might be? I don't know.

Mr. WAXMAN. Well, we will try to provide further clarification and ask you to cooperate with us.

[The following information was received:]

I was asked on May 26 to provide information about "Special Account Number 4" and "Special Account Number 5." No such accounts are currently maintained by or for the Council, and so far as we can determine no such accounts have ever been maintained by or for the Council.

I respectfully request that this letter be included in the record.

Mr. WAXMAN. Well, Dr. Glenn, I thank you for your presentation here today, and as I indicated, we may have you back.

But let me just review what I think we have learned today, not just from your testimony, but from documents that we have put on the record.

The Council for Tobacco Research was started by public relations people, conducted public relations activities such as promoting research results favorable to the tobacco companies. It funded special projects, but did not control the selection. It acknowledged that tobacco companies selected and controlled the special projects. It ac-

knowledged that lawyers for the tobacco companies may have selected the special projects for the tobacco companies.

I want to indicate that in my view this paints a disturbing picture of public relations masquerading as science, and we will look forward to further clarifications to hopefully disabuse us of some of these facts. But I think the documents that we have already put on the record establish much of that case and are really troubling as to whether this is a scientific inquiry as it has been represented.

I thank you very much——

Mr. GLENN. Mr. Waxman, may I ask a question? Are you impugning my integrity?

Mr. WAXMAN. Well, Dr. Glenn, you represent the Council of Tobacco Relations. You don't know much about what went on before you got there. We introduced documents that indicated the kinds of things that were done by the Council. And it didn't just stop before you got there. In 1990 there was a letter to kids at school that indicated—this was a statement that I will submit it to you as Exhibit 15, if we can get that over to you. A letter written by RJR Tobacco Company in 1990 to the principal of the Willow Ridge School in Amherst, N.Y., and RJR is responding to the questions of fifth graders about the health risks of smoking.

I don't know if you are familiar with that letter. Are you?

Mr. GLENN. No, sir.

Mr. WAXMAN. OK. Well, I am going to read to you what they say. I am quoting. "The tobacco industry is also concerned about the charges being made that smoking is responsible for so many serious diseases. Long before the present criticism began, the tobacco industry in a sincere attempt to determine what harmful effects, if any, smoking might have on human health established the Council for Tobacco Research. Over the years the tobacco industry has given in excess of $162 million to independent research on the controversies surrounding smoking.

"Despite all of the research going on, the simple and unfortunate fact is that scientists do not know the cause or causes of chronic diseases reported to be associated with smoking. The answers to these many unanswered controversies surrounding smoking we believe can only be determined through much more scientific research."

Now, this letter illustrates how the tobacco industry uses the Council for public relations purposes to this day when fifth graders ask about the risks of smoking, the existence for the Council for Tobacco Research allows the tobacco companies to say, we don't know and we are still trying to find out.

I am not impugning your integrity, but I am telling you that there is a tremendous gap between your insistence that CTR has not focused on public relations and all of these documents we have put on the record which indicate that the Council for Tobacco Research has been used exactly for public relations and not fully for scientific inquiries.

Thank you for being here, and we will have further opportunities to work together.

That concludes our hearing today and we stand adjourned.

[Whereupon, at 12:55 p.m., the subcommittee was adjourned, to reconvene at the call of the Chair.]

[The following material was submitted for the record:]

AMERICAN CANCER SOCIETY

AMERICAN LUNG ASSOCIATION®

American Heart Association
Fighting Heart Disease and Stroke

Coalition on Smoking OR Health

For Release:
Thursday, May 26, 1994

Contact: Joe Marx, AHA
202/822-9380
Diane Maple, ALA
202/785-3355
Curtis Allen, ACS
404/329-7920

TOBACCO RESEARCH COUNCIL HAS BEEN PART OF TOBACCO INDUSTRY DECEPTION, HEALTH GROUPS SAY

Washington, May 26 --The Council for Tobacco Research has been part of the tobacco industry's shroud of deception, says the American Heart Association, the American Lung Association and the American Cancer Society, united as the Coalition on Smoking OR Health.

"Evidence that has surfaced in tobacco liability cases clearly shows that the Council for Tobacco Research was a linchpin in the tobacco industry's strategy to mislead the public and the Congress about the dangers of smoking," says Scott D. Ballin, chairman of the steering committee of the coalition and vice president, public affairs for the AHA.

Adds Ballin, "The council's role was to provide a front for the tobacco industry's campaign to discredit the medical evidence that smoking causes disease. The council fit perfectly into tobacco companies' primary objectives to sabotage tobacco control legislation and to protect themselves from liability."

Two years ago, the coalition sent a letter to Rep. John Dingell, D-Mich., chairman of the House Energy and Commerce Committee, asking for an investigation to determine if the tobacco industry had lied to Congress about the purpose of the Council for Tobacco Research. The coalition provided Mr. Dingell with internal tobacco industry documents that were made public in two major tobacco liability cases that were heard in the New Jersey federal court system, Cipollone v. Liggett Group, Inc. and Haines v. Liggett Group, Inc.

"Since the 1950s, representatives of the Tobacco Institute, the major tobacco companies, the Council for Tobacco Research and public relations firms representing the tobacco industry have appeared before numerous congressional committees, made statements to the media and conducted widespread public relations campaigns that had no other purpose than to deceive," the letter said.

Says Ballin, "We commend Representative Waxman and his subcommittee for initiating these important hearings. The investigation must continue so that all the facts are brought before the public. But we also need a public policy solution that

-MORE-

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will stem the tobacco epidemic and hold the tobacco industry accountable for its actions. We urge Mr. Waxman's subcommittee to move swiftly to pass legislation to regulate the tobacco industry."

The coalition supports proposed legislation by Rep. Mike Synar, D-Okla., and Rep. Richard Durbin, D-Ill., that would give the FDA full authority to regulate the manufacture, distribution, sale, labeling, advertising and promotion of tobacco products, without having to ban them. The legislation would be consistent with many of the requirements for prescription drugs, including, products containing nicotine, such as nicotine gum and nicotine patches, as well as requirements for foods.

The Coalition on Smoking OR Health was formed in 1982 by the American Cancer Society, the American Heart Association and the American Lung Association to more effectively inform legislators and other public officials about the health consequences of tobacco use. The three health organizations represent more than six million volunteers throughout the United States.

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STATEMENT OF THE COALITION ON SMOKING OR HEALTH
CONCERNING
THE COUNCIL FOR TOBACCO RESEARCH

The Tobacco Industry Research Committee was established with great fanfare in 1954 by the major tobacco industry manufacturers as well as other companies within the tobacco industry. In an advertisement entitled, "A FRANK STATEMENT TO CIGARETTE SMOKERS," which appeared in over 400 newspapers nationwide, the tobacco industry made the following commitments:

> **We accept an interest in people's health as a basic responsibility, paramount to every other consideration in our business.**
>
> **We always have and always will cooperate closely with those whose task it is to safeguard the public health.**
>
> **Regardless of the record of the past, the fact that cigarette smoking today should even be suspected as a cause of a serious disease is a matter of deep concern to us.**

The advertisement went on to indicate that to carry out its responsibility to the health of the American public, the responsible chief officers of the cigarette manufacturing companies, as well as other tobacco industry associations, were establishing the Tobacco Industry Research Committee (later to become the Council for Tobacco Research).

The Tobacco Industry Research Committee (TIRC) was, according to industry statements, "formed in the interest of the public as well as the industry to meet the challenge raised by widely publicized reports in the press purporting to link tobacco smoking with the cause of lung cancer." Tobacco industry testimony and documents were provided to Congress in 1957. In one document entitled, "Statement Concerning the Origin and Purpose of the Tobacco Industry Research Committee and Its Proposed Functions," the tobacco industry indicated that:

> **In light of the foregoing agitation "(that other things such as air pollution might be a factor in lung cancer)" and in the absence of authoritative findings, there is a responsibility on the part of the management of the tobacco manufacturers and others engaged in the tobacco industry to aid in the final determination of this controversy. It is the earnest wish of the industry to encourage competent scientific authority to find ultimate facts which will dispel the present confusion and to communicate authoritative factual information on the subject to the public.**

The document goes on to discuss some of the general duties and responsibilities of the Committee:

> **The purposes and objectives of the committee are to aid and assist research into tobacco use and health, and particularly the alleged relationship between the use of tobacco and lung cancer and to make available to the public factual information on this subject. It is the considered judgment of the committee that its activities shall be confined to the purposes set forth**

> **and that it is in nowise to be considered or to operate as a trade association or to participate in any activity or give consideration to any matters affecting the business conduct or activities of its members, and that its activities in every respect shall conform to law and all decrees or judgments of courts affecting or relating to the tobacco industry.**

In another document submitted to the Congress in 1957 entitled, "Tobacco Industry Research Committee Statement of Policy Containing Conditions and Terms Under Which Project Grants Are Made," the TIRC went on to state further:

> **In so doing "(supporting research concerning tobacco and health)" the TIRC recognizes the importance of independent research by competent investigators.....The Committee desires to have scientists work with the greatest freedom and without domination of any kind. It will make no attempt to direct the administration of the project once started, to influence its course or to control its results other than to be assured that the funds are properly expended for the purposes of the grant and that all findings are to be reported in accordance with the best scientific practice.**

Since the TIRC was formed in 1954, the TIRC and the tobacco industry manufacturers have appeared before Congress time after time to reiterate the independence of the scientific research being conducted with TIRC funds and to reassure the public that when and if it is established that smoking causes disease, the industry will uphold its promise to the public and "do something about it." What follows are several excerpts from testimony provided to Congress:

1. In July of 1957 Dr. Clarence Cook Little, chairman of the science advisory board of the Tobacco Industry Research Committee told the House Committee on Interstate and Foreign Commerce:

> **The announced purposes and objective of the Tobacco Industry Research Committee are to aid and assist research in tobacco use and health and to make available to the public factual information on this subject.... My appointment is annual and it is clearly understood with the Tobacco Industry Research Committee that if, as, and when the slightest pressure as to what type of direction we should take in research or what the publication of the research should be, is evident that my resignation takes effect immediately. I can say truthfully and honestly that during the period that I have worked on this problem, there has not been the slightest effort to "pull punches," to select evidence, or to limit objectives for research.**

2. On June 25, 1964, Bowman Gray, Chairman of the Board of R.J. Reynolds and spokesperson for the tobacco industry testified before the House Committee on Interstate and Foreign Commerce. In addition to his testimony the following exchange took place between him and the Members of the Committee (Mr. MacDonald and Mr. Curtin):

> **Mr. MACDONALD. Sir, I have just one question to ask. I was not here when you gave your statement but I read on page 4 about the Council for Tobacco Research which you say is comprised of eminent medical scientists and grants of over $7 million have been given to that body by the cigarette industry or tobacco industry.**

If that body did come up with the same findings as the Surgeon General did, what would the attitude of the tobacco people be about the present legislation?

Mr. GRAY. To begin with the grantees who receive money under the scientific advisory board; that is, the vehicle which handles these grants, are perfectly free and certainly requested to publish whatever findings they may arrive at in the course of their investigations. These, however, are scientifically and medically oriented and directed research programs and are not concerned with surveys and statistical reports.

* * *

Mr. GRAY. The group that have been handling this money here have made public all the findings, as far as I know, of this research. Up to now none of it has come up with a positive answer which would be in the area that this causes ill health or this is injurious.

Mr. MACDONALD. If they did?

Mr. GRAY. If they did they would bring it out. Then what do we do?

Mr. MACDONALD. Yes, sir.

Mr. GRAY. We get awfully fast to work to see what we can do about it.

* * *

Mr. WILLIAMS. Mr. Curtin?

Mr. CURTIN. Thank you, Mr. Chairman.

Mr. Gray, assuming that it was proven beyond all doubt that cigarette smoking did cause cancer of the lung and bronchitis, would you then feel that the Federal Trade Commission was fair and reasonable in making a request for a notice, such as they have outlined, on all packages of cigarettes?

Mr. GRAY. I believe you assumed that it had been proven beyond doubt that this was a fact; yes, sir.

Mr. CURTIN. You think such a notice would then be justified?

Mr. GRAY. I think you would have a whole lot more than just the Federal Trade Commission Act involved in such a situation.

Mr. CURTIN. Assuming that it was proven, do you think it would be all right for the Federal Trade Commission to require such a notice?

Mr. GRAY. I do not know how you prove this and that is one of the problems. If it is proven that cigarettes are harmful, we want to do something about it regardless of what somebody else tells us to do. And we would to our level best. This is just being human.

3. Eight years later, in February of 1972, Tobacco Institute President Horace Kornegay, appearing before the Consumer Subcommittee of the Senate Commerce Committee stated:

> **Let me state at the outset that the cigarette industry is as vitally concerned or more so than any other group in determining whether cigarette smoking causes human disease, whether there is some ingredient as found in cigarette smoke that can be shown to be responsible and if so what it is.**
>
> **That is why the entire tobacco industry--growers, warehousemen, and manufacturers--since 1954 has committed a total of $40 million for smoking and health research through grants to independent scientists and institutions. That is why the tobacco industry is spending more money in this special field of research than any other single source, Government or private. Despite this effort, the answers to critical questions about smoking and health are still unknown.**
>
> **Let me first briefly review the conduct of the cigarette industry in relation to this continuing and unresolved controversy. Its conduct has been both responsive and responsible to an extent unparalleled in American industry.**

4. At the same hearing, Robert C. Hochett, Ph.D., acting Scientific Director for the Council for Tobacco Research stated:

> **In 1965 and 1969 I described in considerable detail the nature, organization and modus operandi of the Council, and these descriptions were included in the records. My oral statement of 1965 was supplemented by a complete background document outlining the Council's history, organization, scientific program and publications. This also appears in the record and need not be repeated here.**
>
> **My thesis in these previous presentations was that neither tobacco and health research in general, nor that of the Council has established that tobacco use or cigarette smoking in particular is a "major health hazard." My point is that it has not been shown whether, how, to what extent or in whom cigarette smoking can contribute to the etiology (causation) of any disease that is presently a major cause of illness or early decease. I do not find any convincing evidence that either tar or nicotine or any other agent in cigarette smoke has been "incriminated" in relation to any human disease. Consequently, there is not scientific basis on which to establish "maximum acceptable levels of tar, nicotine or other incriminated agents" as proposed in S.1455.**

5. On February 15, 1978 Horace Kornegay, President of the Tobacco Institute, appeared before the Subcommittee on Health and the Environment and stated:

> **Generally, the industry funds scientific research on smoking and health through the Council for Tobacco Research. That organization, or rather its predecessor, was formed in 1954, and its sole purpose is to support <u>independent</u> scientific research. They have what they call a Scientific Advisory Board, composed of well known and qualified people from all over the country, which determines the scientific merits of the grant applications. (Emphasis added.)**

6. In 1982 Edward A. Horrigan, Jr., then the Chairman of the Executive Committee of the Tobacco Institute, came before the same Subcommittee and stated:

> **After three decades of investigation and millions of dollars invested by the government, the Tobacco Industry and private organizations, the smoking and health controversy remains unresolved. The net result of all of this effort has been that no causal link between smoking and disease has been established. That is not merely the opinion of tobacco industry executives. That is scientific fact readily available to anyone willing to make an objective, unemotional study of the existing evidence.**

Mr. Horrigan added:

> **I am saying that science to date after much research including over $100 million funded by our industry, indicates that no causal link has been shown.**

7. During the same hearing Sheldon Sommers, M.D., then the Scientific Director of the Council for Tobacco Research described in the CTR as a **"funding agency for bio-medical research in the area of smoking and health, funded by tobacco manufacturers."** Dr. Sommers then stated that the CTR **"exerts no influence upon the grantees"** who Dr. Sommers stated "may freely publish what they find as they choose."

One year later, Dr. Sommers reappeared before the Subcommittee on Health and the Environment of this Committee and stated:

> **During the past 18 months, I have served as Scientific Director, Council for Tobacco Research - U.S.A., Inc. This organization, funded by the major U.S. cigarette manufacturers, supports basic and applied bio-medical research relating to smoking and health.**
>
> * * *
>
> **The donors of the money and the Council for Tobacco Research give complete scientific freedom to grant recipients in conducting their studies. The grantees are free to publish their findings and report them at professional meetings.**

Dr. Sommers closed his testimony on behalf of the Council for Tobacco Research as follows:

> **Cigarette smoking has not been scientifically established to be a cause of chronic diseases, such as cancer, cardio-vascular disease or emphysema. Nor has it been shown to affect pregnancy outcome adversely. Rapidly accumulating new basic scientific discoveries and reports and the medical literature render the simplistic statements and the proposed bill invalid.**

Forty years after the TIRC and the CTR were established, the tobacco industry continues to claim that there is no established causal relationship between cigarette smoking and disease (including cancer, cardiovascular disease, emphysema, stroke, premature births, etc.). Evidence which first came to light as part of documents released in the Cipollone case and now supplemented by many other internal industry documents indicates that the TIRC and the CTR were nothing but a public relations front for the

tobacco industry, designed to head off any litigation, legislation, and regulations involving the tobacco industry and its products.

A 1965 internal Council memorandum to W.T. Hoyt from Simon O'Shea summarized the history of the Council and its effectiveness as follows:

> **The Council has, during the last two years, passed through a period which was dominated by events surrounding the preparation and issuance of the Surgeon General's Report and subsequently by congressional consideration of cigarette labeling legislation. During this period the general tone of the Council's public information activities has changed considerably and much staff activity has been devoted to assisting with the problems posed by the Surgeon General's Committee and the legislative deliberations.**
>
> **The period of primary focus on governmental and legislative concerns may now be ending. However, the provision of the labeling bill which will require annual reports by various governmental agencies to the Congress undoubtedly will affect policy in the future. We should at the earliest moment try to learn whether these periodic reports will have an effect of continuing to mute the industry's statements in the scientific field. It certainly must be considered that an open program of scientific discussion might draw governmental attacks on the Council.**

A 1972 memorandum from Fred Panzer, Vice President of the Tobacco Institute, to Horace R. Kornegay, President of the Tobacco Institute, summarize the motives and objectives of the industry:

> **For nearly twenty years this industry has employed a single strategy to defend itself on three major fronts - litigation, politics, and public opinion.**
>
> **While the strategy was brilliantly conceived and executed over the years, helping us win important battles, it is only fair to say that it is not - nor was it intended to be - a vehicle for victory. On the contrary it has always been a holding strategy, consisting of:**
>
> **- creating doubt about the health charge without actually denying it,**
> **- advocating the public's right to smoke, without actually urging them to take up the practice, and**
> **- encouraging objective research as the only way to resolve the question of health hazard.**

The memorandum goes on to lay out a strategy for dealing with the tobacco and health issue for the future, including advancing the idea of convincing the public that "cigarette smoking may not be the health hazard that the anti-smoking people say it is because other alternatives are at least probable." A review of all the existing evidence that has come to light indicates that the Council for Tobacco Research, and its predecessor the Tobacco Industry Research Committee, were an important part of the tobacco industry's attempt to mislead the public and the Congress about the dangers of cigarette smoking. The industry's specific purpose was clearly to head off litigation, legislation, and regulation.

For the last forty years the tobacco industry has been able to conduct its business outside the public eye. Unfortunately for the American public and the estimated 10 million people who have since died from cigarette related diseases since 1964, the tobacco industry was able to convince the Congress that regulation of its product was unwarranted, that they voluntarily would conduct "independent" research on the health risks associated with tobacco, openly provide their findings to the public and the Congress, and take appropriate steps to protect the public if such findings found smoking to cause disease.

The evidence that has come to light indicates an urgent need for the federal government to assume both oversight and regulatory control over tobacco products. The special treatment afforded an industry which produces this nation's single most preventable cause of death must come to an end.

THE COUNCIL FOR TOBACCO RESEARCH-U.S.A., INC.

SUPPORTING BIOMEDICAL INVESTIGATION

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JAMES F. GLENN, M.D.
CHAIRMAN AND PRESIDENT
CHIEF EXECUTIVE OFFICER

September 27, 1994

BY HAND

Hon. Henry A. Waxman
Chairman
Subcommittee on Health
and the Environment of the House
Committee on Energy and Commerce
2415 Rayburn House Office Building
Washington, DC 20515-6118

Dear Congressman Waxman:

By way of re-introduction, I am the Chairman, Chief Executive Officer and President of the Council for Tobacco Research -- U.S.A., Inc. (the "Council"). As you will recall, at your invitation I appeared before the Subcommittee on Health and the Environment on May 26, 1994.

At the May 26 hearing, I answered to the best of my knowledge and ability all questions that were put to me. Many of those questions appeared to reflect inaccurate preconceptions or misinformation about the Council and its work. In this letter, I would like to (1) explain how the supplemental information provided in this letter has been limited because we have not had an opportunity to discuss procedural matters with the Subcommittee staff (Part I of this letter), (2) reiterate some of the main points I made during my testimony (Part II), (3) provide further information and documents in response to requests by the Subcommittee (Part III), and (4) clarify several statements that I made to the Subcommittee (Part IV).

I.

The Council has cooperated fully with the Subcommittee and is continuing to do so. Immediately after I testified on May 26, we began the very substantial task of collecting the documents and information that had been requested by members of the Subcommittee.

As you may be aware from discussions with the Subcommittee staff, we have sought to discuss with the Subcommittee staff procedures for the Subcommittee's handling of documents and information provided to it by the Council. In particular, some of the information and documents involve matters that we regard, for one reason or another, as confidential. We expect to provide to the Subcommittee the information that it requested. However, before doing so, we would like to try to reach an understanding with the Subcommittee staff with respect to the Subcommittee's procedures for handling and disclosing materials that we provide to the Subcommittee. Until last week, we had understood that we would have an opportunity to do that. Apparently, however, the Subcommittee has decided to afford such an opportunity to the tobacco companies -- but not to the Council.

It might be helpful for you to know the factual background of this situation. In August, as we neared the completion of the process of collecting information and documents, our counsel, Judah Best of Debevoise & Plimpton, called William Schultz of the Subcommittee staff to arrange a meeting concerning the Subcommittee's procedures for handling materials provided to it by the Council. Shortly before that time, we had learned that since June the Subcommittee staff had been discussing with the tobacco companies the procedures that would govern the companies' production of documents and information to the Subcommittee. Mr. Best advised Mr. Schultz that the Council was prepared generally to be governed by the procedures that were agreed to by the tobacco companies, and was prepared to raise one additional confidentiality issue that is unique to the Council. Mr. Best twice scheduled meetings with Mr. Schultz to be held early in September, but both meetings were postponed. At no time were we advised that a discussion of the Subcommittee's procedures would be inappropriate or unavailable to us.

On September 21, while our counsel was awaiting the rescheduling of the meeting with Mr. Schultz, we were advised for the first time by Ripley Forbes, also of the Subcommittee staff, that the Subcommittee needed to receive information from the Council within a week, without waiting for any discussions about procedures.

Because we believe it is fundamentally unfair to require the Council to provide documents and information without affording us even an opportunity to discuss the Subcommittee's procedures, we are now providing only certain materials to the Subcommittee. This letter describes the balance of the information and documents that the Council has gathered in response to the Subcommittee's requests. Promptly after an understanding has been reached as to these procedural matters, the Council will make these materials available to the Subcommittee. In the interim, with respect to responses to the Subcommittee's requests that are affected by the confidentiality issue, I respectfully request that this letter be included in the record. Earlier today, our counsel explained to Mr. Forbes that we would be proceeding in this way, and Mr. Forbes indicated that it would be appropriate to do so under the circumstances.

I reiterate that the Council will continue to cooperate fully with the Subcommittee in this matter, and that the Council does not object to providing full and complete information or documents to the Subcommittee. Rather, our concern arises from the possible disclosure to others of non-public information and documents without any procedures to control such disclosure, and from the possible impact of such disclosure on pending litigation against the Council and on the legitimate privacy interests of others.

II.

Preliminarily, I would like to provide you with some of the basic facts about the Council.

The Council and its forerunner have awarded more than $230 million in grants-in-aid and contracts to independent research institutions and scientists for scientific research. The Council, which is funded primarily by five major American cigarette manufacturers, is now awarding approximately $19.5 million in research grants annually.

Scientific research funded by the Council has included grants to leading scientists (including three Nobel laureates), who are affiliated with many of the country's most distinguished research institutions. (These research institutions are listed in one of the attachments to my written testimony to the Subcommittee, dated May 25, 1994.) Most of the researchers funded by the Council were also receiving support from funding organizations such as the National Institutes of Health, the American Cancer Society, the American Heart Association, and the National Cancer Institute.

The research funded by the Council relates to issues of smoking and health. The focus of much of this research is the etiology of diseases associated with smoking. To a considerable extent, meaningful research into the etiology of those diseases involves basic research into disease mechanisms, much of which takes place at the cellular and sub-cellular level. Accordingly, in recent years, an increasing proportion of the research funded by Council grants-in-aid has been devoted to such basic research. That trend is consistent with developments in scientific research. It is this kind of basic scientific research that much of the scientific community believes will provide answers to questions about the causes of chronic diseases and about the relationship of smoking to those disease mechanisms.

The researchers who receive Council grants are selected on the basis of ratings given to their applications by the Council's Scientific Advisory Board ("SAB"). The members of the SAB have been, and are, distinguished scientists of unimpeachable integrity.

The researchers who receive Council grants conduct their research independently, without control by or interference from the Council. They are expected to publish their research findings in scientific journals, again without interference from the Council. Over 5,000 such articles have been published, the vast majority of them in peer-reviewed journals, as a result of research funded by the Council's grants and contracts.

To the best of my knowledge, none of the results or findings from research sponsored by the Council (including research funded as Council Special Projects) has been kept secret or has been suppressed in any way. The Council

has not asserted any privilege with respect to the results of, or the findings from, any such scientific research.

III.

Together with this letter, I am submitting on behalf of the Council an Appendix and four boxes of documents. I explain below the contents of the Appendix, of the four boxes of documents, and of the information and documents that we are not now providing, as discussed in Part I.

Publications by Nobel laureates (requested in May 26, 1994 Transcript ("Tr.") at p. 54). As I testified on May 26, the Council has funded three investigators who have won Nobel Prizes: Dr. Baruj Benaceraff of Harvard University, Dr. Stanley Cohen of Vanderbilt University and Dr. Harold E. Varmus of the University of California at San Francisco.

Dr. Benaceraff, who was awarded the Nobel Prize in 1980, received a Council grant from 1972 through 1974 for investigating "Control of Specific Cellular and Humoral Immune Responses to Neoplastic and Non-neoplastic Tissues." Item A in the Appendix includes three publications acknowledging the Council's support of Dr. Benaceraff's research.

Dr. Cohen, who was awarded the Nobel Prize in 1986, received a Council grant from 1987 through 1993 for investigating "The Role of Lipocortin in the Cellular Response to EGF." Item B in the Appendix includes six publications acknowledging the Council's support of Dr. Cohen's research.

Dr. Varmus, who was awarded the Nobel Prize in 1989, received a Council grant from 1984 through 1986 for investigating "Functional Analysis of Cellular Oncogenes Activated During Tumorigenesis." Item C in the Appendix is a publication acknowledging the Council's support of Dr. Varmus' research.

As I explained to the Subcommittee on May 26, the Council-funded research by these Nobel laureates was basic biomedical research aimed at improving our understanding of fundamental disease processes -- which is the kind of re-

search that is now believed to further scientific understanding of the effects of tobacco use on health. Dr. Benaceraff conducted pioneering research into the humoral immunological response of the host when presented, attacked or invaded by cancerous growths. His work has provided important insights into how regulatory mechanisms may operate in defense of the host organism. Dr. Cohen studied cell growth factors and their role in regulating growth and differentiation. His investigation of genetic controls of growth factors opened the door to our understanding of mechanisms by which normal cells become cancerous. Dr. Varmus' pioneering work with oncogenes made important contributions to our overall understanding of how healthy cells become transformed into cells that can no longer control their growth and therefore become cancerous.

Information sent to grant applicants (Tr. at p. 65). Item D in the Appendix is a copy of a form letter, with attachments, that is provided by the Council to successful grant applicants. One of these attachments, "Important Procedural Information for Grantees," refers specifically to publications by grantees. Item E in the Appendix is the Council's Statement of Policy, which is sent to all grant applicants. The Statement of Policy makes it clear that the Council expects grantees to report their findings in medical and scientific journals, and requests that any publications acknowledge the Council's support.

Our Statement of Policy also says, in very clear terms: "The Council desires to have scientists work with the greatest freedom, without domination of any kind. It will make no attempt to direct the administration of a project once started, to influence its course or to control its results . . . ." That is the Council's fundamental policy: to give complete scientific freedom to its grantees, and to let the chips fall where they may.

List of Council Special Projects (Tr. at pp. 47, 106). As I explained in my testimony, Council Special Projects were research projects that the Council's sponsors wished to fund. Tr. at 46. These research projects were funded by the sponsors, and were administered by the Council, separately from the grant-in-aid program.

We have prepared a list of all Council Special Projects for which the Council has a file. That list in-

cludes the following information for each such project (where such information is available from the Council's files or from published sources): (a) the name of the principal investigator or investigators, (b) the institution or institutions with which the principal investigator or investigators were associated, (c) the title or subject matter of the Council Special Project, (d) the dates of funding of the Council Special Project, (e) the total amount of funding provided by the Council, and (f) a list of the publications that apparently resulted, or may have resulted, from the Council Special Project. Some of the publications identified on the list appear in the Council's Special Projects files; others have been collected from other sources. In a number of instances, it is not clear whether a particular publication resulted from Council Special Project funding.

My statement at the May 26 hearing that 250 peer-reviewed articles are believed to have resulted from Council Special Projects was based on my information about the number of publications that either were in the Council's files or have been collected from other sources. Several clarifications should be made to that statement. First, our list sets forth over 400 articles or presentations that resulted or may have resulted from Council Special Projects; so far, I understand, copies of about 250 of these articles or presentations have been obtained, and that understanding was the source of my statement at the hearing. Second, most but not all of these 250 articles or presentations were peer-reviewed. Third, abstracts relating to Council Special Projects publications were not included in the Council's Annual Reports.

We expect to provide this list to you promptly after we have reached an understanding with the Subcommittee staff with respect to procedures for the Subcommittee's handling of such materials provided by the Council. In the interim, I respectfully request that this letter be included at pages 47 and 106 of the May 26 transcript.

Statements by Ms. Cohen (Tr. at p. 78). At the May 26 hearing, I was asked to supply documentation for my statements about Dorothea B. Cohen, the former Council employee to whom comments were attributed in the Wall Street Journal article of February 11, 1993. We had intended to respond to the Subcommittee's request for documentation by obtaining an affidavit from Ms. Cohen, setting forth her

view that the Wall Street Journal article was inaccurate. However, Ms. Cohen has moved, and we have been unable to locate her. We have spoken with Dr. John E. Bevilacqua, Ms. Cohen's treating neurologist (who is also her cousin).

Dr. Bevilacqua has provided us with a letter dated August 20, 1994, describing Ms. Cohen's medical condition as of that date and as of February 11, 1993, when the Wall Street Journal article appeared. Dr. Bevilacqua has asked that his letter be treated as confidential, in deference to Ms. Cohen's privacy interests. We expect to provide Dr. Bevilacqua's letter to the Subcommittee promptly after we have reached an understanding with the Subcommittee staff with respect to procedures for the Subcommittee's handling of materials provided by the Council. In the interim, I respectfully request that my letter be included at page 78 of the May 26 transcript.

I have learned that I was mistaken when I testified on May 26 that, following the publication of the Wall Street Journal article, Ms. Cohen called the Council and apologized to one of our employees for the statements attributed to her in the article. What happened was that shortly after the Wall Street Journal article was published, Ms. Cohen was contacted on our behalf and said that she had been misquoted in the article. The fact that Ms. Cohen had stated that she had been misquoted in the article was reported to an officer of the Council, who in turn reported that to me. As a result, I formed the mistaken impression that Ms. Cohen had called the Council, but my basic understanding about what she did say was correct.

Financial information (Tr. at p. 82). We have prepared three separate tables setting forth the dollar amounts contributed in each year, by each contributor, to the Council and to the Tobacco Industry Research Committee ("TIRC") for the General Fund, for Council Special Projects, and for the Council's Literature Retrieval Division ("LRD"). (I understand that LRD was a division of the Council from 1971 until 1983, that LRD compiled medical literature for the use of the tobacco companies, and that LRD's assets were transferred in 1983 to LS, Inc., a corporation that is unrelated to the Council.) This financial information is nonpublic, and the Council's members regard it as confidential. We expect to provide these tables to the Subcommittee promptly after we have reached an understanding with the

Subcommittee staff with respect to procedures for the Subcommittee's handling of materials provided by the Council. In the interim, I respectfully request that this letter be included at page 82 of the May 26 transcript.

We have collected copies of the audited financial statements of the Council and its predecessor for each year from 1963 through 1993. (In 1983, the Council changed from a calendar year to a November 1 fiscal year.) We have also collected copies of budgets for each year from 1954 through 1962; we are unable to locate financial statements from before 1963. Again, this financial information is non-public, and the Council and its members regard it as confidential. We expect to provide these tables to you promptly after we have reached an understanding with the Subcommittee staff with respect to procedures for the Subcommittee's handling of materials provided by the Council. In the interim, I respectfully request that this letter be included at page 82 of the May 26 transcript.

Item F in the Appendix is a copy of the Council's current by-laws. Article III of the by-laws provides the method of apportioning the funding of the Council among its sponsors.

MAI contracts (Tr. at p. 70). Item G in the Appendix includes copies of each of the Council's contracts with Microbiological Associates, Inc. ("MAI"), together with contract renewals. The Council spent some $12 million under the MAI contracts on a large-scale, long-term study of the effects of smoking inhalation on mice.

I was mistaken when I told the Subcommittee that these contracts contained no restriction on publication by MAI. The Council has had no research contracts during my tenure, and I had erroneously assumed that the Council's policies with respect to publication by contract researchers were the same as its policies with respect to publication by grantees. Since my testimony, I have learned that the MAI contracts provided that the Council's prior written approval was required for MAI to publish its research findings. Such provisions are customary in research contracts.

It is my understanding that the results of the major inhalation study performed by MAI were published in complete and unedited form. In addition, MAI published

dozens of articles based on its Council-funded research. Item H in the Appendix is a list of 89 publications or abstracts that appear to have resulted from the Council's support of MAI, at least 73 of which acknowledge support from the Council.

Council employees (Tr. at p. 85). We have prepared a list setting forth the names, years of employment and the current (or terminal) position of employees of the Council and TIRC from 1954 to the present. I should advise you that while our staff expended considerable time and effort in trying to compile a list of all Council employees, the list may not be complete or totally accurate because the Council's records for this 40-year period are incomplete.

In deference to the privacy interests of the persons whose names appear on this list, we regard it as confidential. We expect to provide this list to the Subcommittee promptly after we have reached an understanding with the Subcommittee staff with respect to procedures for the Subcommittee's handling of materials provided by the Council. In the interim, I respectfully request that this letter be included at page 85 of the May 26 transcript.

Studies associating smoking and diseases (Tr. at p. 59). At the hearing, I was asked about studies funded by the Council that found that tobacco use increased the likelihood of disease. With all due respect, this request is extremely naive, and therefore very difficult to respond to meaningfully. Modern scientific studies into the etiology of chronic diseases typically focus on narrow questions, the answers to which contribute to a broader understanding of disease processes. However, as a general matter, each such study, standing alone, does not state that smoking does or does not make the chronic disease more likely. The reported research findings have implications for the relationship between smoking and disease that are far more subtle, complex and cumulative.

Consequently, in many instances, it is difficult to determine -- and it ultimately is a subjective matter -- whether a publication is deemed to have found an increased likelihood of disease. Indeed, I believe that any two persons who might review the full set of publications resulting from the Council's grants in response to this request would come up with different sets of documents. As I stated on

May 26 in response to this request, abstracts of publications resulting from CTR grants and contracts have appeared in the Council's annual reports, and we can make the publications themselves available to the Subcommittee for its review.

With these qualifications, we are providing in the boxes marked "Box 1" and "Box 2" copies of over 375 publications resulting from Council-funded research that could be considered to indicate that tobacco use may increase the likelihood of developing diseases or conditions that have been associated with smoking. (These documents were selected from the Council's files of publications resulting from Council grants. Those files are not complete since not all publications have been provided by the researcher or located by the Council.) We have used our best efforts to compile for the Subcommittee a complete set of such publications, in light of the difficulties referred to above. In addition, in order to reduce the burden on the Subcommittee, we are not providing copies of publications that simply rely on or refer to previous research findings associating smoking and diseases, and in a number of instances we are not providing copies of publications that are preliminary to, or repetitive of, publications that are being provided.

Nicotine studies (Tr. at pp. 61, 62). The two boxes of documents marked "Box 3" and "Box 4" contain copies of over 560 publications resulting from Council-funded research that appear to examine the effects of nicotine. (As explained above, the set of publications from which these documents were selected is incomplete.) Again, we have used our best efforts to compile for the Subcommittee a complete set of such publications.

As I mentioned during my testimony on May 26, during the very week of my testimony the Council sponsored an important seminar on central nervous system receptors, including the receptors that respond to nicotine and its analogues. Item I in the Appendix includes copies of the program from that seminar and of the abstracts presented at that seminar.

Council Special Projects files (Tr. at p. 106). We have gathered 14 boxes of documents, consisting of about 30,000 pages, from the Council's files on Council Special Projects. The vast majority of these documents are from

files that are arranged alphabetically by the name of the principal investigator or, in some cases, the investigator's institution. There are also documents from files containing financial information about Council Special Projects and documents from Special Project desk files of certain Council employees. Approximately one-third of these pages consist of applications and pre-publication reports by researchers, or evaluations of a researcher or of his or her research. We believe that the information that is reflected in these documents was provided to the Council with a reasonable expectation of confidentiality, and we therefore regard these documents as confidential.

We expect to be able to provide all these documents to you promptly after we have reached an understanding with the Subcommittee staff with respect to procedures for the Subcommittee's handling of materials provided by the Council. In the interim, I respectfully request that this letter be included at page 106 of the May 26 transcript.

In addition, I am advised that there are 54 documents from these Council Special Project files that are subject to claims of attorney-client privilege, attorney work-product protection or joint defense privilege asserted by the Council or its sponsors. We do not intend to provide 51 of these documents to the Subcommittee, and we intend to redact the other three. None of these documents constitutes a researcher's report of his or her results or findings. (As stated above, the Council has not asserted any privilege with respect to such results or findings; and my understanding is that none of the Council's sponsors have done so.) No communications with scientific researchers are being withheld on privilege or work-product grounds.

"Special Accounts" (Tr. at pp. 115-16, 117). I was asked on May 26 to provide information about "Special Account Number 4" and "Special Account Number 5." No such accounts are currently maintained by or for the Council, and so far as we can determine no such accounts have ever been maintained by or for the Council.

I respectfully request that this letter be included at pages 116 and 117 of the record.

Blanket request (Tr. at p. 99). At the hearing, Mr. Synar asked me to provide "all materials that are cen-

tral to this hearing prior to 1987" and "all of the materials available in the [Council's] files." Tr. at p. 98. I responded that the Council would cooperate fully "and would provide whatever you require." Tr. at p. 99. I did not understand Mr. Synar to be asking for every piece of paper in the Council's files. Rather, I thought he was having me confirm that we would be responsive to the Subcommittee's requests. Indeed, I have no way of knowing what documents Mr. Synar regards as "central to this hearing." And it certainly would not be feasible for the Council to produce all of its files to the Subcommittee. We estimate that those files include over 2.5 million pages, and I respectfully submit that it would serve no purpose to deluge the Subcommittee with documents beyond those that the Council has already gathered in response to the Subcommittee's broad requests.

I respectfully request that this letter be included at page 99 of the record.

IV.

I would also like to clarify several points that I made during my testimony on May 26.

I was questioned on May 26 about documents that are exhibits to the Majority Staff Report, dated May 26, 1994, and entitled "The Hill and Knowlton Documents: How the Tobacco Industry Launched Its Disinformation Campaign." As I testified, I had never seen Exhibits 9 and 10 to that Report, which appear to be documents prepared by Hill & Knowlton in 1954. Tr. at 49, 51-52. To reiterate, these documents and the events they describe predate my tenure at the Council by three decades. Following the hearing, we reviewed the Council's files, and as a result we have learned that, contrary to my belief as of May 26, the Council's files do contain copies of Exhibit 9 and of a portion of Exhibit 10.

Reviewing the exhibits to the Majority Staff Report indicates to me, as a reader of these documents in 1994, that Hill & Knowlton provided resources to help organize TIRC and gave assistance to TIRC's public relations efforts during its early years. In hindsight, I do not find it surprising that documents prepared by TIRC's public rela-

tions advisors tend to focus on public relations. By the same token, it is not surprising that the minutes of Scientific Advisory Board meetings from the same period discuss almost exclusively matters of scientific research and the award of research grants by TIRC, with virtually no reference to TIRC's public relations activities. (At its September 20, 1954 meeting, for example, the Scientific Advisory Board discussed and adopted a Statement of Policy for TIRC that closely resembles Item E in the Appendix, including policies about scientific freedom and publication.) I have no reason to believe that the public relations activities reflected in these documents had any effect on TIRC's program of funding scientific research.

The Council has not been involved in such public relations activities during my tenure or, to the best of my knowledge, for many years prior to my association with the Council. Today, the Council's contacts with the media and the public are limited to advising them of the Council's research-funding activities in a general way, and advising the scientific community of its grantees' activities through the issuance of its annual reports. It remains my strong belief, based on my personal knowledge and my conversations with others, that the Council as I know it, and as it has existed for decades, has had as its principal function the sponsorship of scientific research into questions of tobacco use and health.

I testified that the SAB is "really" the decisionmaker with respect to funding by the Council, but did not explain precisely the Council's decisionmaking process. Tr. at 84. It currently works as follows:

1. When a full, formal application for a grant-in-aid is received by the Council, it is assigned to two SAB members (and, on occasion, an outside reviewer) for review and evaluation. The full SAB then rates each application on a numerical scale. The Council's scientific staff then prepares a list of these applications in an order that reflects the SAB's numerical ratings.

2. As a technical matter, I have the final authority to award grants-in-aid. As a practical matter, however, I defer very heavily to the SAB's numerical ratings, and those ratings are by far the predominant

factor in determining grant awards. After each SAB meeting, the Council's scientific staff and I review the SAB's numerical ratings. We may reduce the amounts of some awards, either as directed by the SAB or in order to permit the funding of additional grants. On rare occasions, we diverge slightly from strict adherence to the SAB's numerical ratings -- for example, to improve the balance of the Council's research program among various scientific disciplines. The SAB is fully aware of this procedure, and it is informed of the final funding decisions at each meeting when it approves the minutes of its previous meeting.

I advised the Subcommittee that the Council has been sued in a number of cases and that no court has made a finding of liability against the Council. After stating that the jury in the Cipollone case had rejected the allegations of fraud regarding the Council, I answered "yes" to Congressman Greenwood's question as to whether a court had found for the Council as a defendant. Tr. at 64. That answer was substantially correct, both in that (1) the Cipollone jury rejected allegations of a conspiracy to defraud involving the Council and (2) in several cases courts have granted motions for summary judgment dismissing cases brought against the Council. In fact, however, the Council was not a defendant in Cipollone.

Finally, I wish to make it clear that my testimony about the relationship between tobacco use and health reflected only my personal views, and not those of the Council. The Council as a body takes no position on these issues.

* * *

I trust that this letter and the documents and information that are either enclosed with or described in this letter respond adequately to the Subcommittee's questions about the Council. We remain willing to continue to cooperate with the Subcommittee and its staff to address any further inquiries that you may have.

Respectfully yours,

James F. Glenn, M.D.

Enclosures

THE HILL and KNOWLTON DOCUMENTS: HOW THE TOBACCO INDUSTRY LAUNCHED ITS DISINFORMATION CAMPAIGN

A Staff Report, Majority Staff
Subcommittee on Health and the Environment

This majority staff report of the Subcommittee on Health and the Environment analyzes documents that describe in detail the formation and early years of the Tobacco Industry Research Committee, a joint tobacco industry group now known as the Council for Tobacco Research.

The ostensible purpose of the Tobacco Industry Research Committee was to provide "aid and assistance to the research effort into all phases of tobacco use and health." In a full-page advertisement run in over 400 newspapers on January 4, 1954, the major tobacco companies explained that they formed the Research Committee because they "accept an interest in people's health as a basic responsibility, paramount to every other consideration in our business."

The documents obtained by the Subcommittee were written by top officials at the Hill and Knowlton public relations firm, an advisor to the Tobacco Industry Research Committee during its formative years. The documents show that contrary to the industry's public assertions, the real purpose of the Tobacco Industry Research Committee was to "sponsor a public relations campaign which is ... entirely 'pro-cigarettes.'" The goal was "reassurance of the public" through "communication of ... the existence of weighty scientific views which hold there is no proof that cigarette smoking is a cause of lung cancer." The public relations campaign was so extensive that in 1955 the Tobacco Industry Research Council hired 35 staff members of Hill and Knowlton to conduct the campaign.

The documents describe in detail the massive campaign undertaken from 1954 through 1956 by the Tobacco Industry Research Committee to influence public opinion. They explain how during these early years the Tobacco Industry Research Committee:

- transformed obscure scientific reports favorable to the industry into headline news across the country;
- courted the editors of the nations' major news organizations, advising them in personal meetings of "the need for editorial responsibility in handling stories that rouse unwarranted fears";
- influenced the content of news reports in major newspapers, magazines, and television shows, including the New York Times, the Washington Post, and the Edward R. Murrow Television Show;
- planned a 17-step public relations campaign to respond to one particularly unfavorable report;
- influenced medical opinion by sending hundreds of thousands of copies of booklets prepared by the

Tobacco Industry Research Committee to "all doctors" in the United States;

- established "personal liaisons" in organizations like the American Medical Association and American Cancer Society to secure "advance information ... concerning research" and "first-hand knowledge of the theories, methods, and personalities of those involved in research on tobacco and health"; and

- ultimately succeeded in shifting national opinion, so that by 1956 Hill and Knowlton could report that "neither the press nor the public seems to be reacting with any noticeable fear or alarm to the recent attacks."

As recounted by one Hill and Knowlton executive in 1953, the chief executive officers of the leading tobacco companies were "emphatic in saying that the entire activity is a long-term, continuing program, since they feel the problem is one of promoting cigarettes and protecting them from these and other attacks that may be expected in the future." Forty years later, the Council for Tobacco Research is still in operation and the campaign of disinformation continues.

Chronological Summary of Key Documents

December 1953. Dr. Earnest Wynder and his colleagues at the Sloan-Kettering Institute in New York City publish research showing that cigarette tar condensate causes fatal cancers when painted on the skin of mice. The research study, a copy of which is attached as exhibit 1, attracts massive media coverage.

December 15, 1953. The chief executive officers of the nation's largest tobacco companies meet on the morning of December 15, 1953, at the Plaza Hotel in New York City to discuss the implications of the new health research. Hill and Knowlton executives attend the meeting and, later in the day, write a memorandum summarizing the meeting. The memorandum is attached as exhibit 2.

The meeting is unprecedented: it is the first time the CEOs had met together outside of occasional dinners honoring an industry leader. In attendance were Paul M. Hahn, President, American Tobacco Company; Joseph F. Cullman, Jr., Chairman and President, Benson & Hedges; O. Parker McComas, President, Philip Morris & Co.; and J. Whitney Peterson, President, U.S. Tobacco Company.

At the meeting, the CEOs agree that the health criticisms are "extremely serious" and "worthy of drastic action" (p. 3). According to the memorandum, "the officials stated that salesmen in the industry are frantically alarmed and that the

decline in tobacco stocks on the stock market has caused grave concern" (p. 4).

According to the memorandum, "the chief executive officers of all the leading tobacco companies -- R.J. Reynolds, PM, B&H, U.S. Tobacco Company, B&W -- have agreed to go along with a public relations program on the health issue" (p. 1).

Specifically, they agree that:

> "They should sponsor a public relations campaign which is positive in nature and is entirely 'pro-cigarettes.' ... They are also emphatic in saying that the entire activity is a long-term, continuing program, since they feel the problem is one of promoting cigarettes and protecting them from these and other attacks that may be expected in the future. Each of the company presidents attending emphasized the fact that they consider the program to be a long-term one." (p. 2)

December 24, 1953. Less than two weeks later, on December 24, 1953, Hill and Knowlton writes a set of "Preliminary Recommendations for Cigarette Manufacturers." This document is attached as exhibit 3.

The paper observes:

> "[T]he grave nature of a number of recently highly publicized research reports on the effects of cigarette smoking ... have confronted the industry with a serious problem of public relations. ... The situation is one of extreme delicacy. There is much at stake and the industry group, in moving into the field of public relations, needs to exercise great care not to add fuel to the flames." (pp. 1-2)

According to Hill and Knowlton:

> "The recommended approach is conservative and long-range. ... There is no public relations nostrum, known to us at least, which will cure the ills of the industry with one swallow. The need is for a soundly conceived and effectively executed program based upon continuing research and factual information." (p. 2)

Hill and Knowlton recommended:

> "The underlying purpose of any activity at this stage should be reassurance of the public through wider communication of facts to the public. It is important that the public recognize the existence of weighty scientific views which hold there is no proof that cigarette smoking is a cause of lung cancer." (p. 2)

In particular, Hill and Knowlton recommended that the tobacco manufacturers take "joint action" by establishing a "Tobacco Research Committee" headquartered in New York City (p. 3).

Hill and Knowlton recommended that:

> "The first public statement of the Committee should be designed to clarify the problem and to reassure the public that: (a) the industry's first and foremost interest is the public health; (b) there is no proof of the claims which link smoking and lung cancer; and (c) the industry is inaugurating a joint plan to deal with the situation." (p. 4)

This statement should be "plaçed as an advertisement in leading newspapers" (p. 4).

January 4, 1954. The CEOs followed the advice of Hill and Knowlton on January 4, 1954, running a full-page advertisement in newspapers across the country. This advertisement is attached as exhibit 4.

The advertisement is called "A Frank Statement to Cigarette Smokers." It announces the formation of the Tobacco Industry Research Committee to provide "aid and assistance to the research effort into all phases of tobacco use and health."

In the advertisement, the tobacco companies assert:

> "We accept an interest in people's health as a basic responsibility, paramount to every other consideration in our business. ... We always have and always will cooperate closely with those whose task it is to safeguard the public health."

January 15, 1954. Hill and Knowlton writes a "Progress Report" of activities. This progress report is attached as exhibit 5.

The progress report states that the "Frank Statement" appeared in 448 newspapers, reaching a circulation of 43,245,000 in 258 cities. The advertisement was run in virtually all cities with a population above 50,000. The total cost was $257,276.

May 3, 1954. Hill and Knowlton reports to the Tobacco Industry Research Committee on a booklet, "A Scientific Perspective on the Cigarette Controversy." The report is attached as exhibit 6.

According to the report, 205,000 copies of the booklet were printed. The booklet was sent to 176,000 doctors. The booklet and an accompanying press release were also sent to 15,000 editors and reporters.

June 21, 1954. Hill and Knowlton writes a "Public Relations Report and Recommendations for the Tobacco Industry Research Committee." The report is attached as exhibit 7.

By June 21, 1954, the Tobacco Industry Research Committee had selected a scientific advisor (Dr. Clarence Cook Little, a former director of the American Cancer Society) and a scientific advisory board. According to Hill and Knowlton, with these steps in place:

> "The Committee now has the basis needed for carrying on a long-range plan of public relations activities. ... These activities will endeavor to keep the following facts before the Public:
>
> 1. That there is no proof that smoking is a cause of lung cancer;
> 2. That an impartial and independent Board of scientists, doctors and educators is advising the TIRC, as a public service, on all aspects of tobacco use and health;
> 3. That the TIRC is determined, through a long-range program, to make every possible effort to help get the facts through laboratory and statistical research." (p. 2)

August 17, 1954. Hill and Knowlton sends T.V. Harnett, the Chairman of the Tobacco Industry Research Committee, a "Confidential Report of Activities through July 31, 1954." The confidential report, and an accompanying cover letter, are attached as exhibit 8.

The cover letter to Harnett calls the report "highly confidential" and "request[s] that you retain it only for your personal consideration." The letter warns that "no additional copies be made and that this copy not be placed in files."

The report itself is 24 pages long and describes many details of the public relations campaign being run by the Tobacco Industry Research Committee.

The report makes it clear that Hill and Knowlton -- not the independent scientists -- actually ran the Tobacco Industry Research Committee. According to the report:

> "Since the Committee had no headquarters and no staff, Hill and Knowlton, Inc. was asked to provide a working staff and temporary office space. As a first organizational step, public relations counsel assigned one of its experienced executives, W.T. Hoyt, to serve as account executive and handle as one of his functions the duties of executive secretary for the Tobacco Industry Research Council." (p. 3)

The report further states that Hill and Knowlton "provided

assistance in selecting" the Scientific Advisory Board (p. 3), "proposed" Dr. Little for the Scientific Director (p. 3), and "handled liaison, agendas, organizational plans, business affairs, reports, and materials for meetings of the TIRC [and] the Scientific Advisory Board, ... in addition to developing operating procedures for the research program" (p. 5).

The report provides a "case history" that describes how the Tobacco Industry Research Committee would transform an obscure scientific report favorable to the industry into national headline news (pp. 7-9). According to the case history, "advance checking" by TIRC revealed that Dr. Hueper was scheduled to give an unpublicized report "concerning the lack of a proven link between lung cancer and smoking" in July in Sao Paulo, Brazil. TIRC reproduced the report and two pages of highlights and established a "special liaison" in Sao Paulo "to give word of Dr. Hueper's delivery as quickly as possible, so as to enable distribution of the talk while it was still newsworthy." As soon as the talk was given, "personal delivery of the Hueper release was made to important newspapers and services as well as distribution to science writers, editorial writers and feature writers." In the end:

> "Although may of the writers covering the Sao Paulo meeting failed to mention the Hueper talk in their dispatches, it is significant that, as a result of the distribution in the U.S.A., stories questioning a link between smoking and cancer were given wide attention, both in headlines and stories. In some press accounts, the Hueper story took precedence over the reports of Drs. Hammond and Wynder, even though the latter were made available to the press in advance of their delivery on a hold-for-release basis."

The report describes many other efforts of the Tobacco Industry Research Committee to influence media, including "special personal contacts" with Time, Newsweek, U.S. News and World Report, and Business Week (p. 9); preparation of editorials entitled "The Same Old Culprit" and "Truth Makes a Slow Crop" that were "widely used in 'home town' dailies and weeklies throughout the country" (p. 10); and "assistance ... provided to the New York Times for a Sunday Magazine piece ... on "Why People Smoke," which discussed some of the now-abandoned old charges against cigarettes" (p. 12).

In many instances, the Tobacco Industry Research Committee worked behind the scenes to influence the content of individual articles. In one case, the intervention of TIRC resulted in "seven revisions and five qualifying additions" to a story in Cosmopolitan magazine that "was already in type" (p. 10).

In other cases, it was quicker and more effective simply to hire free-lance authors to write favorable articles for the Tobacco Industry Research Committee:

> "Especially-written articles are being developed that can be used or adopted for use in various media receptive to or seeking material relating to the subject. ... To achieve this objective more quickly and effectively, the free lance services of qualified science writers are being used." (p. 23)

Another important function of the Tobacco Industry Research Council was to infiltrate anti-smoking organizations to obtain "advance information." According to the report:

> "Personal contacts are advantageous not only in disseminating and gathering information but for enlisting support and advice on problems. ... Personal liaison has been established in such cancer, research, and medical organizations and associations as the American Medical Association, American College of Chest Physicians, American Cancer Society, Sloan-Kettering Foundation, New York University School of Industrial Medicine, National Cancer Institute, International Cancer Congress' Cancer Prevention Committee, as well as with individual doctors and scientists. These continue to make possible obtaining advance information or papers concerning research being done in this and related fields." (pp. 17-18)

Moreover, "individual coverage of medical and scientific meetings such as the AMA meeting in San Francisco have resulted in first-hand knowledge of the theories, methods, and personalities of those involved in the research on tobacco and smoking" (p. 19).

October 7, 1954. Hill and Knowlton writes a "confidential memorandum" describing "Tobacco Industry Research Committee Information Activities" in August and September 1954. The memorandum is attached as exhibit 9.

The memorandum describes "recent major public relations projects" from August through September 1954. According to the memorandum, the Scientific Director and Chairman of the Tobacco Industry Research Committee met with the following publishers to "explain the industry's long-range intention to support a research program devoted primarily to the public interest": Arthur Hays Sulzberger, the president and publisher of the New York Times; Helen Rogers Reid, chairman of the board of the New York Herald Tribune; Jack Howard, president of Scripps-Howard Newspapers; William Randolph Hearst, Jr., president and publisher of the Hearst Consolidated Publications; and Roy E. Larsen, president of Luce Publications (p. 1).

The memorandum describes how the Tobacco Industry Research Council influenced the content of the Edward R. Murrow Television Show:

> "A conference was held with Edward R. Murrow, Fred Friendly, his producer, ... at the Tobacco Industry Research Committee offices in the Empire State Building. ... The Murrow staff emphasized the intention to present a coldly objective program with every effort made to tell the story as it stands today, with special effort toward balanced perspective and concrete steps to show that the facts still are not established and must be sought by scientific means such as the research activities the Tobacco Industry Research Committee will support. Mr. Murrow was assured of continued cooperation from the Tobacco Industry Research Committee to the extent possible under the scope of the TIRC program." (p. 2)

The memorandum describes how an article being prepared by Leonard Engle for Harper's magazine "use[s] TIRC as a source of information" and "should lend weight to the industry's contention that there is no proof of the charges and that there are many other factors that enter strongly into the increasing incidence of lung cancer" (pp. 2-3). It also reports that in the Washington Post "a feature story by Nate Haseltine us[es] long excerpts from paper by Dr. Hueper, which was supplied him in personal contact through Hill and Knowlton, Inc., Washington office" (p. 3).

Finally, the memorandum describes the tactic of hiring free-lance authors to write ostensibly independent articles favorable to the industry, reporting that "C.B. Colby, free lance popularizer of science, was retained for research and possible writing of article concerning all the hazards of modern life which people are cautioned against and leading to the conclusion that in spite of all the death scares, "You Still Live Longer" (p. 4).

November 26, 1954. John W. Hill, the founder of Hill and Knowlton, writes a memorandum to Hartnett, the chairman of the Tobacco Industry Research Committee, on "Proposed Budget for 1955." The memorandum is attached as exhibit 10.

According to the memorandum, "the budget for staff operations provides for the use of all or part of the time of 35 different staff members of Hill and Knowlton, Inc." (p. 1). This compares with 23 Hill and Knowlton staff who were hired in 1954.

The memorandum also explains that the budget includes $70,000 to print 200,000 copies of a booklet describing the Tobacco Industry Research Council for distribution to "all doctors" and $250,000 for "one nationwide advertisement reporting to the public at the end of TIRC's first year."

All told, in 1954 the Tobacco Industry Research Committee spent $477,955 on payments to Hill and Knowlton and on advertising -- slightly over 50% of the organization's entire

budget. In 1955, the public relations and advertising expenditures were budgeted to increase by 13% to $539,400. In 1994 dollars, this would represent an expenditure of over $2.5 million.

April 28, 1955. Hill and Knowlton writes a confidential "Public Relations Report" to the Tobacco Industry Research Council. The report is attached as exhibit 11.

The report finds that after a year of intensive public relations activities, "progress has been made" (p. 1). Specifically:

> "The first "big scare" continues on the wane. There is much general awareness of the big IF factors involved. ... Treatment of the cigarette-health issue in public media continues to improve from the Tobacco Industry Research Committee point of view. Even adverse stories now tend to carry modifying statements. Positive stories are on the ascendancy." (pp. 1-2)

However, the report also warned that "the next major public problem" will be a report by Drs. Hammond and Horn, scheduled for release at a conference of the American Medical Association in June in Atlantic City:

> "There is no reason to hope that the .. report will be in any way better than the one last year. There is no reason to hope that it will not result in widespread attention in the press. The A.M.A. meeting this year is closer to the major news centers than it was last year in San Francisco."

May 25, 1955. One month after warning about the upcoming Hammond-Horn report, Hill and Knowlton sends the Tobacco Industry Research Committee a "rundown of the status of certain steps being taken in anticipation of the June 6 presentation of the second Hammond-Horn report." The rundown is attached as exhibit 12.

The report from Hill and Knowlton details a 17-step program for anticipating and responding to the Hammond-Horn report. Among the steps outlined in the report are harvesting the results of the Tobacco Industry Research Council's earlier contacts with the Edward R. Murrow television show. Step 8 calls for "provid[ing] all the assistance possible in making the two Murrow shows, scheduled for May 31 and June 7, as timely and positive as possible" (p. 2). Step 9 is "transcribing pertinent sections of the Murrow show immediately after its presentation, and providing copies of these transcripts to major news outlets in New York early in the morning following the show" (p. 2).

February 14, 1956. Hill and Knowlton writes another

confidential "Public Relations Report" to the Tobacco Industry Research Committee. A copy of the report is attached as exhibit 13.

The report finds that the activities of the Tobacco Industry Research Council have shifted public opinion in favor of the tobacco industry and succeeded in isolating many of the industry's critics. According to the report:

> "A large proportion of the attacks against smoking made recently, and expected to continue in the next few months, originate with the same small group of critics who have led the anti-tobacco moves of the past two or three years. Neither the press nor the public seems to be reacting with any noticeable fear or alarm to the recent attacks." (p. 1)

The report also notes the success of the program to influence medical opinion:

> "A factor that has become more noticeable ... is that, more and more, doctors and scientists are voluntarily speaking up at medical meetings to express disagreement with the flat charges made against tobacco. They do not exonerate tobacco but say that the case against smoking has not been proved and that much more evidence is needed." (p. 2)

Furthermore:

> "Another aspect that also is becoming more apparent is the great emphasis being placed by scientists in this country and abroad on the role of air pollution as the major cause of lung cancer. Two recent scientific reports on air pollution and health received national newspaper attention. The subject is being treated by the press as a new, interesting and important phase of the overall situation." (p. 2)

Despite these important successes, the memorandum warns against "any attitude of complacency in our public relations approach, especially when we consider ... it is not possible at this time to assess fully the probable impact of federal government reports and activities that are indicated in the months ahead" (p. 1).

July 19, 1956. Hill and Knowlton writes a confidential memorandum to Hartnett, the chairman of the Tobacco Industry Research Committee, regarding "Conferences with Life and Reader's Digest. The memorandum is attached as exhibit 14.

According to the memorandum, Dr. Little of TIRC met with the Deputy Managing Editor of Life, Robert T. Elson, on July 17. At the meeting:

"Dr. Little ... pointed out the importance to the public of receiving a balanced presentation of all the facts and underscored the need for editorial responsibility in handling stories that rouse unwarranted fears." (p. 1)

The next day, on July 18, Dr. Little met with DeWitt Wallace, the editor of Reader's Digest. At this meeting:

"Dr. Little stressed the importance of the public not being stampeded into undue fears and the great responsibility held by major publications to keep the public adequately informed so that they would not tend to over-simplify the problem and expect a "push-button answer" to problems so complex as cancer and heart disease." (p. 2)

Exhibit 1

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Experimental Production of Carcinoma with Cigarette Tar*

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The increasing frequency of primary cancer of the lung in many parts of the world has aroused great interest in this condition and has stimulated a search for an explanation. In 1950, Wynder and Graham (40), on the basis of a clinical and statistical investigation, presented evidence of a real association between lung cancer and smoking, especially of cigarettes. These data have been well substantiated by a large-scale British study by Doll and Hill (9, 10). Both studies showed that the risk of developing cancer of the lung increases in direct proportion to the amount of smoking. Ten other recent studies reached similar conclusions (8, 11, 15, 20, 21, 24, 26, 33, 34, 42). In 1952, The Council of International Organizations of Medical Sciences convened a symposium on the endemiology of lung cancer and agreed that the present evidence points to a relationship between lung cancer and cigarette smoking (12).

Tobacco is also thought to play some role in the production of cancer of the larynx, oral cavity, and esophagus. Although the studies of those relationships are not so complete as the studies on lung cancer, the collected data are suggestive (33, 41).

The increasing incidence of bronchiogenic carcinoma and the available evidence relating smoking to it and possibly to cancer of other sites led us to undertake the experimental work reported here. This investigation is directed toward determining in laboratory animals whether there are carcinogenic factors in cigarette smoke.

Previous Investigations

Many attempts have been made with tobacco products to induce cancers in a variety of experimental animals. The first was reported by Broech in 1900 (4). He painted guinea pigs with tobacco "juice" for an unknown period of time and described epithelial proliferation. Subsequently, many different approaches to the problem were undertaken with various types of tobacco, different methods of tar preparation, and different species of animals. Many of these studies were carried on for too brief a period of time or with too few animals to be regarded as significant. Hoffmann and his associates (17), for instance, painted animals for only 14 days, at which time they noted hair loss. Wacker and Schmincke (37) observed proliferation of epithelium in rabbits' ears 21 days after a subcutaneous injection of pipe tar.

The first recorded experiment with mice and with tobacco tars as the suspected carcinogen was the one just cited by Hoffmann and co-workers. The more detailed of the subsequent studies are listed in Table 1. This table attempts to summarize the methods used in the various studies and the results obtained. In many instances the method of study was not described in sufficient detail to give all the information considered essential.

From this survey of the literature it is found that, before our study, all the previous attempts to produce experimental cancer in mice with tobacco products were successful in the production of only seven epidermoid cancers of the skin.

Several investigators attempted to induce pulmonary tumors in mice with tobacco smoke. Lorenz and co-workers (22) obtained negative results in this manner. Campbell (5), and especially Essenberg (13), however, claim to have found a significantly higher percentage of pulmonary adenomas in the experimental than in the control group. It is doubtful that such a finding is important. At any rate, so far these methods have not induced true bronchiogenic carcinomas.

The majority of the investigators working with tobacco tars used rabbits as the experimental animals (14, 23, 27-32, 36). In view of the fact that the present work deals with mice we shall only briefly list some of the studies with rabbits. Rolle reported the production of carcinomas in rabbit ears after painting the ears with a distillate of tobacco (28, 30, 32). Sugiura (36), in attempting

* This investigation was supported by a research grant from the National Cancer Institute of the National Institutes of Health, Public Health Service.

† Present Address: Memorial Center for Cancer and Allied Diseases, 444 East Sixty-eighth Street, New York 21, N.Y.

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man carcinogen, is present in tobacco, but recent studies by Daff and co-workers (8) based on the arsenic content of various types of European tobacco tends to place less emphasis on this inorganic element. Heat, cigarette paper, flavoring, and wetting agents have been suggested as etiologic factors in the production of cancer, but it must be noted that clinical evidence has also pointed to cigar-smoking, pipe-smoking, and tobacco-chewing as possible factors in the production of cancer of the respiratory and alimentary tract.

The actual carcinogenic agent or agents in tobacco remain to be identified. Studies combining chemical and biologic efforts leading to their identification are urgently needed. Should one be able to identify definite carcinogens and succeed in removing them, or at least in reducing their quantity in tobacco, proper preventive methods would be at hand. Such studies may further our understanding of human and animal carcinogenesis and may lead to the development of practical preventive measures against cancer.

SUMMARY AND CONCLUSIONS

1. A cigarette tar condensate was obtained with a smoking machine which simulated human smoking habits. The resulting tar was dissolved in acetone and applied to the backs of CAF_1 mice in a dosage of 40 mg. of tar/acetone solution 3 times a week. Control mice were painted with acetone.

2. Of 81 tarred mice, 59 per cent developed papillomas. The first lesion was noted in the 53d week, and the mean time of appearance was 66 weeks.

3. Of 81 tarred mice, 44 per cent developed histologically proved carcinomas. The first carcinoma was observed in the 49d week, and the average time of appearance was 71 weeks. Of 62 mice alive at 12 months, 58 per cent developed cancer. Seventy-one weeks constitutes approximately one-half of the life span of CAF_1 mice. This corresponds roughly with the fact already noted that in the human about 30–35 years of smoking, or approximately one-half the life span, are required for the production of bronchogenic carcinoma.

4. One carcinoma was transplanted for 4 generations and another one is currently growing in the 13th generation.

5. Control mice painted with acetone alone showed no skin lesions. At the end of 20 months of painting, 53 per cent were still living, compared to 9.8 per cent in the group painted with tobacco tars.

6. The group of mice painted with croton oil in addition to the tar, starting in the 7th month, cannot be properly evaluated because of a greater number of deaths occurring during the 12th and 14th months, although within the period of observation no acceleration of cancer formation was noted.

7. The group of mice started with acetone and receiving croton oil beginning in the 7th month showed roughening and thickening of the epidermis, but no tumor formation was noted.

8. All CAF_1 mice painted with 0.3 per cent solution of methylcholanthrene in acetone developed cancer within 4½ months. The first papilloma appeared during the 6th week, with average appearance during the 7th week. The first carcinoma was observed during the 12th week, with a mean time of appearance of 16 weeks.

9. The results obtained with CAF_1 mice establish condensed cigarette tar as a carcinogen for mouse epidermis. These studies provide a tool to determine and isolate the possible carcinogenic agent(s) within tobacco tar. At present it is not known which fraction or fractions in tobacco tars are carcinogenic. Combined chemical and biologic studies are now in progress to search for such agents. Such studies, in view of the corollary clinical data relating smoking to various types of cancer, appear urgent. They may result not only in furthering our knowledge of carcinogenesis, but in promoting some practical aspects of cancer prevention.

ACKNOWLEDGMENTS

The authors wish to express their gratitude to Colin B. Cook, Mary Gay Crow, and Gertrude Canal of Washington University School of Medicine, Department of Surgery, St. Louis, Mo., for their technical assistance.

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Hill & Knowlton

Exhibit 8

Hill Client 039
F. Folsom Mss

December 15, 1953

HK 60

BACKGROUND MATERIAL ON THE CIGARETTE INDUSTRY CLIENT

The following information was given us by the presidents of the leading tobacco companies at the Hotel Plaza this morning.

I. Participants

There is no trade association in the cigarette industry. This is because the tobacco companies are prevented by the dissolution decree of 1911 and the criminal convictions under the Anti-Trust Act in 1939 from carrying on many group activities.

As a matter of fact, before the current health crisis arose, cigarette manufacturers never met together at any time except at dinners honoring some industry leader.

The group was called together by Mr. Paul Hahan, President of the American Tobacco Company. The chief executive officers of all the leading companies - R. J. Reynolds, Philip Morris, Benson & Hedges, U. S. Tobacco Company, Brown & Williamson - have agreed to go along with a public relations program on the health issue.

Liggett & Myers is not participating in the organization because that company feels that the proper procedure is to ignore the whole controversy.

In addition to the cigarette companies, the two important groups of tobacco growers involved are enthusiastically supporting the new program. Together these tobacco growers represent some 600,000 farms and 2,700,000 farmers. Obviously, the tobacco growers are the political strength along with the 1,300,000 retail tobacco outlets. The tobacco growers will be represented by officials of the grower organizations.

II. Organization

Because of the anti-trust background, the companies do not favor the incorporation of a formal association. Instead, they prefer strongly the organization of an informal committee which will be specifically charged with the public relations function and readily identified as such.

For example, Mr. Hahn reported that one name they had considered was the "Tobacco Industry Committee for Public Information." John Hill suggested that he felt the word "research" should appear along with "information" in the title of the committee.

III. The Industry's Position

The industry is strongly convinced that there is no sound scientific basis for the charges that have been made. They believe that the more sensational accusations in the recent papers were premature and in some cases represent publicity issued in the hopes of attracting funds and support for further research.

They point out that the National Cancer Institute of the U. S. Public Health Administration, which is a government agency and supported by Congressional appropriations, has officially refuted the tie-up between cigarette smoking and cancer.

Nevertheless, they realize that the industry should not engage merely in a defensive campaign, replying to and answering individual research papers or magazine articles.

They feel that they should sponsor a public relations campaign which is positive in nature and is entirely "pro-cigarettes." They are confident they can supply us with comprehensive and authoritative scientific material which completely refutes the health charges.

They are also emphatic in saying that the entire activity is a long-term, continuing program, since they feel that the problem is one of promoting cigarettes and protecting them from these and other attacks that may be expected in the future. Each of the company presidents attending emphasized the fact that they consider the program to be a long-term one.

IV. Responses to Questions

The companies' answers to questions put them by John Hill and the undersigned provide valuable background. They are as follows:

> Will the cigarette companies organize themselves into an association publically announced, which will openly sponsor their public relations activities?

The companies replied that they had no desire to set up a smoke screen or "front" type of organization. They are perfectly willing to sponsor any statements that may be issued or any institutional advertising that may be recommended and approved.

Do they accept the principle that public health is paramount to all else, and would they issue a public statement spelling this out?

Everyone present wholeheartedly agreed to this principle and readily consented to widespread dissemination of a sound statement of principles.

Distribution of such a statement it was agreed would probably be the first step in the public relations program that Hill and Knowlton would recommend.

Do the companies consider that their own advertising and competitive practices have been a principal factor in creating a health problem?

The companies voluntarily admitted this to be the case even before the question was asked. They have informally talked over the problem and will try to do something about it. They do, however, point out that this is the one important public relations activity that might very clearly fall within the purview of the anti-trust act. Accordingly, it is doubtful that we will be able to make any formal recommendation with regard to advertising or selling practices and claims.

Will the companies agree to sponsor new research which will provide definite answers to the charges?

A clear-cut answer to this question was deferred for the time being. The companies all say that they are carrying on much more research in their own laboratories and are sponsoring more research at hospitals and universities than is generally recognized. They believe that when we are acquainted with all of the scientific and factual material in the hands of the companies, we will agree that the major problem is to disseminate information on hand rather than to conduct new research.

However, John Hill did not agree to this and emphatically warned the companies that they should probably expect to sponsor additional research.

Do the companies view this problem as being extremely serious and worthy of drastic action?

The answer is obvious since the companies have met together for the first time since 1939, since they have promptly proceeded to retain Hill and Knowlton, and are already considering such expensive techniques as the use of institutional advertising. They recognize the possibility that it might be desirable to use institutional advertising to promote the basic statement.

As another indication of how serious the problem is, the officials stated that salesmen in the industry are frantically alarmed and that the decline in tobacco stocks on the stock exchange market has caused grave concern, especially since tobacco earnings will be much higher next year because of the termination of excess profits taxes.

Are we primarily concerned with cigarettes rather than all tobacco?

There can be no doubt but that the problem is cigarettes and the task is to get out information concerning cigarettes. The attacks have all been against cigarettes. Of course, it is true that the attacks now made on cigarettes will eventually be made against all tobacco if not stopped, and it is also true that anything done in favor of cigarettes will be favorable to all tobacco.

Another reason why the emphasis should be on cigarettes is that there are existing trade associations in the cigar and tobacco field. They are all jealous of their prerogatives and if we stick to cigarettes we will avoid all such complications.

IV. Other Information

The current plans are for Hill and Knowlton to serve as the operating agency of the companies, hiring all the staff and disbursing all funds. The chairman will probably be Mr. Hahn or the head of one of the other companies resident in New York. There will be a strong subcommittee of chief executives, all resident in New York.

Tommy Ross, counsel for American Tobacco Company, has almost completed a "white paper" on the scientific facts involved in the health issue which he will make available to us for use or inclusion in something we will want to distribute to all the press, magazines, etc.

It was arranged for Hill and Knowlton to interview the scientific directors of all the leading companies. Three interviews are being held today, December 15, at 12:30, 2:30 and 4 p.m. respectively. Another will be held on Wednesday.

Following completion of the scientific interviews we will interview Tommy Ross, Ben Sonenberg (counsel for Philip Morris), and Sidney J. Wayne Associates (counsel for Lorillard).

It was also suggested that we might want to interview the advertising people, although the company presidents indicated that the advertising agencies did not have a great deal of material bearing upon the controversy. They thought it most important for us to see the scientific directors and the public relations people mentioned.

The Question of Polls:

The presidents indicated that they had thought about the possibility of a public opinion poll. We agreed that such a poll might prove to be necessary, and also indicated that a poll of certain important groups such as the doctors themselves and teachers might be desirable. Clearly, it is necessary to know: (a) the awareness of the problem, and (b) the extent to which the charges are believed, before extensive action is recommended.

Present at the Meeting:

Paul M. Hahn	President, American Tobacco Company
Joseph F. Cullman, Jr.	Chairman and President, Benson & Hedges
O. Parker McComas	President, Philip Morris & Co., Ltd., Inc.
J. Whitney Peterson	President, U. S. Tobacco Company
- - - -	P. Lorillard Company

BCG:AO

Bert C. Goss

Exhibit 3

Hill/ 329 MK 1
MRC 1953

December 24, 1953

PRELIMINARY RECOMMENDATIONS FOR
CIGARETTE MANUFACTURERS

Because of the grave nature of a number of recently highly publicised research reports on the effects of cigarette smoking, widespread public interest has developed, causing great concern within and without the industry.

These developments have confronted the industry with a serious problem of public relations. Obviously, that problem would be quickly solved if the adverse publicity would cease and people would stop talking about the whole matter.

But there is no evidence that the publicity has abated, or is about to abate, or that the research workers who are critical of cigarettes are going to cease these criticisms. A check among national magazines indicates that other periodicals are considering articles on the subject. Among them are Woman's Home Companion, Look and Cosmopolitan. The February issue of Pageant has an article publicising the Wynder researches.

There is nothing the manufacturers can say or refrain from saying that can stop people from being interested in their health, nor allay their fear of cancer. So long as the causes and cure of this dread disease remain unknown people will be subject to waves of fear regarding it.

It is important that the industry do nothing to appear in the light of being callous to considerations of health or of belittling medical research which goes against cigarettes.

The industry should lose no time in making it completely clear to the American people that it is not unmindful of the public health.

There is an evident urgency about the matter which makes it advisable to suggest certain immediate steps. A fully rounded-out program

will be developed when there has been enough time to make a more comprehensive study of additional aspects of the problem and to think through various courses of action and projects.

The situation is one of extreme delicacy. There is much at stake and the industry group, in moving into the field of public relations, needs to exercise great care not to add fuel to the flames.

The recommended approach is conservative and long-range. We do not believe the industry should indulge in any flashy or spectacular ballyhoo. There is no public relations nostrum, known to us at least, which will cure the ills of the industry with one swallow. The need is for a soundly conceived and effectively executed program based upon continuing research and factual information.

It would be a mistake for the industry group to inaugurate the contemplated program unless it is prepared to maintain it for a minimum of three years. The results of some of the medical research suggested could hardly be in hand short of that period of time.

The underlying purpose of any activity at this stage should be reassurance of the public through wider communication of facts to the public. It is important that the public recognize the existence of weighty scientific views which hold there is no proof that cigarette smoking is a cause of lung cancer.

In connection with the proposed activity, it is impossible to overlook the fact that some of the industry's advertising has come in for serious public criticism because of emphasis on health aspects of smoking.

This, of course, is a problem for the individual companies and will not be included in this program. But it must be recognized that some of the advertising may have created a degree of skepticism in the public mind which at the start at least could affect the believability of any public relations effort.

The decision of a group of companies in the industry to take joint action needs to be implemented by the selection of a Chairman and Treasurer and the adoption of procedures for the collection and disbursement of funds. In addition, it is important that the group establish procedures for expeditious clearance of any policy statements it may decide to issue.

The following recommendations are submitted for consideration by the manufacturers:

1. Headquarters of the Committee. Headquarters should be established in New York City.

2. Name of Committee. The following name is submitted: Tobacco Research Committee.

3. Set-up and function of Committee. The word "research" should be included in the name of the Committee to establish the fact that the group will carry on or sponsor fundamental scientific research and will not be solely an information agency. The Committee's research should be of two kinds:

(a) scientific, medical research

(b) editorial and statistical research into pertinent phases of the current controversy.

The Committee should be prepared on competent scientific advice from outside the industry to give substantial support to objective non-duplicating medical research that is most likely to be productive promptly of convincing results.

The Committee should have a Director of Research, a medical research authority of unquestioned national repute. The Director would have such research assistants as may be required. The Research Director would serve as spokesman for the Committee on medical and scientific matters.

The Committee should also form an Advisory Board composed of a group of distinguished men from the fields of medicine, research and education. These should be men whose integrity is beyond question.

The Director of Research and the Advisory Board should be consulted by the Committee on these points:

a. What areas of objective medical research should be undertaken? Should it be confined to the problem of lung cancer or extend to other aspects of cigarette smoking and health?

b. How and where and under what auspices should the industry carry out its joint research effort? Should a Research Foundation be established which would finance research projects by existing laboratories and institutions, and if so, which ones? Or should the industry establish a new jointly financed research laboratory to carry on the work?

c. How much money, in the opinion of the Committee's Director of Research and its Advisory Board, should the member companies appropriate for medical research undertaking?

4. Public Statement by cigarette makers. The first public statement of the Committee should be designed to clarify the problem and to reassure the public that: (a) the industry's first and foremost interest is the public health; (b) there is no proof of the claims which link smoking and lung cancer; and (c) the industry is inaugurating a joint plan to deal with the situation.

This statement should be:

(a) distributed widely as news, and to employees, stockholders, distributors, tobacco growers, dealers, suppliers, public officials, national and community leaders and other groups;

(b) placed as an advertisement in leading newspapers and in leading news magazines.

(Draft of suggested copy of statement is attached.)

5. Research Sub-committee. A scientific research sub-committee should be set up by the top committee to be composed of Research Directors

of member companies for the purpose of:

a. working with the Committee's Director of Research;

b. reviewing scientific materials assembled for public information;

c. initiating scientific material for educational use by the Committee.

6. Continuing Public Relations Research. There should be set up at the headquarters of the Committee, under the direction of the Research Director, a continuing research project to collect, coordinate and disseminate (where practical) available information on various medical research activities bearing on pertinent phases of cigarettes and health. As time permits, this project would explore such questions as:

a. Why do mice show no tendency to develop lung cancer in experiments where they live half their lives in smoke-filled chambers?

b. Why, in some experiments, do mice show a tendency to develop skin cancer, when painted over a period with tobacco tars - whereas efforts to produce lung cancer in mice, by keeping them immersed in tobacco smoke, have failed?

c. Why has the rise in lung cancer been most marked among men, although the greatest rise in the use of cigarettes in the last 25 years seems to have been among women?

d. Why does the rate of lung cancer vary so greatly between certain cities, although the per capita rate of cigarette consumption in these cities seems approximately the same?

e. What is the correlation, if any, between lung cancer and certain changes in American life - such as steadily increased industrialization, increased urbanization, and the rising problem of atmospheric pollution in many of our urban centers?

f. Why is cancer of the lung on the increase, whereas no such rise appears in similar illness of the tongue, lip or throat?

g. Is the incidence of lung cancer less in rural areas than it is in urban areas, and if so what is the per capita consumption of cigarettes in these respective areas?

h. Is the incidence of lung cancer greater in cold climates than in mild climates and in the south, and if so what is the per capita consumption of cigarettes in the respective areas where this differential seemingly occurs?

i. The figures of the Damon Runyon Cancer Fund estimate in 1952 twenty-two thousand deaths from lung cancer in the United States in an estimated population of over one hundred fifty million individuals. The report in the New York Herald Tribune as of Sunday, December 13th, quoted the British Medical Society as advising that there were thirteen thousand cases of lung cancer in Great Britain last year. With Britain approximately one-quarter the size of the United States, their incidence of lung cancer would be approximately four times as great as the United States. What are the facts about this and what is the incidence of climate, etc. in the development of lung cancer?

j. Is it possible that England, with a larger percentage of lung cancer incidence, may possible have obtained this result due to the fact that the tobacco for their cigarettes is not treated in any way with casing? Should the efficacy of casing used in the manufacture of American cigarettes be studied as possibly an antidote to the deleterious effects of tobacco, if any?

k. With the extension of human life due to miracle drugs, etc. what is the percentage of the increase of lung cancer, if any, comparable to other diseases during the past ten years?

l. What may be the effect on the significance of statistical comparisons of more accurate diagnosis during the past few years into specific causes of death?

✓ m. What are the benefits and enjoyment derived from smoking, both by scientific tests and by measurement of smoker reactions and attitudes?

✓ n. What are the smoking habits of long-lived distinguished public leaders?

✓ o. What are the human ills erroneously attributed to tobacco over the centuries?

There are many similar lines of inquiry which have so far been pursued without definitive answers. They should be explored still more vigorously, and with still greater resources; and the results studied for their usefulness as a matter of public information.

7. Public Opinion Poll. A national survey of public opinion is

* needed to determine attitudes toward cigarettes and tobacco held by (a) the medical profession; and (b) the public at large. The results of such

a poll should be helpful in developing more effectively the continuing program of public information that may be required to offset anti-cigarette propaganda and to give justified reassurance to the public.

8. White Paper. The Committee should distribute as soon as possible a scientific White Paper digesting current available opinion of authorities on cigarette smoking and lung cancer.

9. Relations with the Press. An important function of the Committee will be to see that the pertinent facts are made available to the press.

In addition to any current statements or releases that may be issued, background memoranda of facts may be circulated to the press when occasion requires. The Committee, of course, will be alert to what is being published or said on the subject of concern to the industry and if any misstatements appear, the facts will be offered to proper sources.

In the case of magazines, the facts will be placed in the hands of editors for such use as may suit their purposes. Available for this work will be the publicity staff of public relations counsel. Any publicity activities, of course, will be adapted to current needs and opportunities as indicated by trends in public and professional opinion and discussions.

10. Radio and Television. Millions of people are informed and their attitudes influenced by radio and television. It will be important to keep commentators and other key people in broadcasting aware of the Committee's existence and of any facts it may assemble.

Moreover, the Committee should be on the alert for public discussion programs where spokesmen for the facts as the Committee sees them might be welcome. Public relations counsel has a radio and television specialist who can function in this area.

Plans should be explored for giving attention to the positive aspects of smoking through motion pictures suitable for television use as well as group showings.

11. Committee as a source of facts. The work of the Committee in the field of public information should be such as to establish the Committee as a reliable source of industry facts on this subject, and a flow of enquiry by mail, telephone and personal visitation most likely can be expected gradually to develop. The Committee should develop as rapidly as possible materials, data and statistics bearing on various aspects of the cigarette industry, and have adequate staff to insure meticulous attention to all enquiries from the press or public.

12. Information for special groups. Attention should be given to material on cigarettes going to special groups such as women's clubs, garden clubs and other organizations that have discussion and study programs, and corrections offered in the case of any misinformation noted.

13. Washington Activities. The Washington office and staff of public relations counsel will be available to place accurate and up-to-date information into the hands of appropriate Committees of Congress, Congressmen and Senators from tobacco states, and interested government officials.

14. Materials for company distribution. It is extremely important that the facts and views as developed by the Committee be communicated promptly to various elements within the industry itself. Employees, stockholders, distributors, growers and others should know the facts in order that they can speak intelligently when the subject is discussed in their own groups.

15. Medical Groups. The Committee will need to keep abreast of programs of various medical associations and groups.

16. Cooperation of other groups. The Committee should explore and develop to the greatest extent that it can, the possibility of cooperation from allied groups such as growers, retailers and distributors.

CONCLUSION

As already noted, it has not been practical to develop a full program in the brief space of time available. The effort has been to outline a basic policy approach to the problem and to indicate the direction which the activity should take in implementing policy.

We believe that the correct path to follow is one of patient, continuing, sure-footed presentation of the facts to the public -- facts supported and documented by careful research.

THE NEW YORK TIMES, MONDAY, JANUARY 4, 1954.

Exhibit 4

A Frank Statement to Cigarette Smokers

RECENT REPORTS on experiments with mice have given wide publicity to a theory that cigarette smoking is in some way linked with lung cancer in human beings.

Although conducted by doctors of professional standing, these experiments are not regarded as conclusive in the field of cancer research. However, we do not believe that any serious medical research, even though its results are inconclusive, should be disregarded or lightly dismissed.

At the same time, we feel it is in the public interest to call attention to the fact that eminent doctors and research scientists have publicly questioned the claimed significance of these experiments.

Distinguished authorities point out:

1. That medical research of recent years indicates many possible causes of lung cancer.

2. That there is no agreement among the authorities regarding what the cause is.

3. That there is no proof that cigarette smoking is one of the causes.

4. That statistics purporting to link cigarette smoking with the disease could apply with equal force to any one of many other aspects of modern life. Indeed, the validity of the statistics themselves is questioned by numerous scientists.

We accept an interest in people's health as a basic responsibility, paramount to every other consideration in our business.

We believe the products we make are not injurious to health.

We always have and always will cooperate closely with those whose task it is to safeguard the public health.

For more than 300 years tobacco has given solace, relaxation, and enjoyment to mankind. At one time or another during those years critics have held it responsible for practically every disease of the human body. One by one these charges have been abandoned for lack of evidence.

Regardless of the record of the past, the fact that cigarette smoking today should even be suspected as a cause of a serious disease is a matter of deep concern to us.

Many people have asked us what we are doing to meet the public's concern aroused by the recent reports. Here is the answer:

1. We are pledging aid and assistance to the research effort into all phases of tobacco use and health. This joint financial aid will, of course, be in addition to that already being contributed by individual companies.

2. For this purpose we are establishing a joint industry group consisting initially of the undersigned. This group will be known as TOBACCO INDUSTRY RESEARCH COMMITTEE.

3. In charge of the research activities of the Committee will be a scientist of unimpeachable integrity and national repute. In addition there will be an Advisory Board of scientists disinterested in the cigarette industry. A group of distinguished men from medicine, science, and education will be invited to serve on this Board. These scientists will advise the Committee on its research activities.

This statement is being issued because we believe the people are entitled to know where we stand on this matter and what we intend to do about it.

TOBACCO INDUSTRY RESEARCH COMMITTEE

500 FIFTH AVENUE, NEW YORK 36, N. Y.

SPONSORS:

THE AMERICAN TOBACCO COMPANY, INC.
Paul M. Hahn, President

BENSON & HEDGES
Joseph F. Cullman, 3d, President

BRIGHT BELT WAREHOUSE ASSOCIATION
F. S. Royster, President

BROWN & WILLIAMSON TOBACCO CORPORATION
Timothy V. Hartwell, President

BURLEY AUCTION WAREHOUSE ASSOCIATION
Albert Clay, President

BURLEY TOBACCO GROWERS COOPERATIVE ASSOCIATION
John W. Jones, President

LORILLARD COMPANY, INC.
P. Lorillard, Jr., President

P. LORILLARD COMPANY
Herbert A. Kent, Chairman

MARYLAND TOBACCO GROWERS ASSOCIATION
Samuel S. Lawson, General Manager

PHILIP MORRIS & CO., LTD., INC.
O. Parker McCollum, President

R. J. REYNOLDS TOBACCO COMPANY
E. A. Darr, President

STEPHANO BROTHERS, INC.
C. S. Stephano, Sr., Director of Research

TOBACCO ASSOCIATES, INC.
(An organization of tobacco growers)
J. B. Hutson, President

UNITED STATES TOBACCO COMPANY
J. W. Fornton, President

Exhibit 5

Hill Exhibit 821
F: Hearings Hi,

January 15, 1954

HK55

PROGRESS REPORT

I. ADVERTISING

The Committee statement, entitled "A Frank Statement to Cigarette Smokers," appeared in 448 newspapers, reaching a circulation of 43,245,000 in 258 cities. This included, with very few exceptions, all cities of 50,000 or more population, plus all plant or headquarters cities of Committee members. Total cost for newspaper space will be approximately $244,304. Cost of three press publications (EDITOR AND PUBLISHER, PUBLISHERS' AUXILIARY AND AMERICAN PRESS) will be approximately $2,113. Production costs will add $3,040 to this.

In addition to the above cost covered in the $250,000 appropriation, a cost of $4,213 was incurred to transmit by telegram the revised list of sponsors and the prescribed change in headline.

On authorization by the Chairman, 11 tobacco industry publications were added to the list and received the same two-page version of the advertisement which appeared in the press publications. Total cost of space and preparation for this will be approximately $3,606.

This will make the total advertising expenditure, not including reprints, $257,276.

To date 200,000 reprints of the advertisement have been ordered by the companies.

Additional Advertising Solicitation

The question of extending the advertising to appear in a variety of additional publications was suggested, in some instances by Committee members and, in others, by direct solicitation from the publications. These included the food and drug trades; the negro and labor press as well as the foreign language press; and the news weeklies -- Time, Newsweek, and U. S. News.

It is our recommendation that no further advertisement be placed using the original statement, and that the above suggested groups of publications be carefully considered in relation to any subsequent plans for new advertisements. The circulation of all the above groups, with the possible exception of the foreign language press, can be considered to have been reached in large measure by the original daily newspaper advertising.

II. REQUEST FOR REPRINTS FROM N.A.T.D.

Mr. Kolodny of the National Association of Tobacco Distributors has indicated he is willing to distribute the statement advertisement to 1,000,000 tobacco dealers throughout the country.

In tabloid size, production of 1,000,000 reprints would cost about $3,000.

III. PRESS RELEASE AND PRESS COVERAGE

The press release announcing formation of the Committee was given national distribution and was widely covered by newspaper, radio, TV and the magazines.

Typical clippings of this coverage have been sent to Committee members.

Editorial comment was most favorable, th editorials still being received from all over the country.

IV. INFORMATION AND CORRESPONDENCE

During the first week after appearance of the ad, we handled many personal and telephone calls, including professional men offering services, crackpots and others. These were in addition to the many inquiries from the networks and the press.

During the first two weeks after the appearance of the ad, over 1,000 telegrams and letters were received at Hill and Knowlton offices. A preliminary analysis indicates that objective or pro-tobacco comments run better than two to one.

V. MEETING OF COMPANY RESEARCH DIRECTORS

Chairman Hahn called a meeting of Research Directors of the tobacco companies on Thursday, January 7. A report on this meeting will be presented to the Tobacco Industry Research Committee.

VI. "WHITE PAPER"

A draft of the "White Paper" was submitted to the Research Directors Advisory Committee and suggestions from these officials are being coordinated into a revised draft for final clearance.

VII. CALLS ON ADVERTISING AGENCIES

Messrs. Hill, Goss and Littin have called on senior executives of the principal advertising agencies to obtain their suggestions and comments. In addition, a meeting of the Research Directors of advertising agencies was called to discuss the matter of a poll and depth survey.

Exhibit 6

May 3, 1954

HK47

TO: TOBACCO INDUSTRY RESEARCH COMMITTEE

RE: Report on TIRC booklet, "A Scientific Perspective on the Cigarette Controversy"

The booklet, "A Scientific Perspective on the Cigarette Controversy," was released April 14, 205,000 copies being printed. It was sent to 176,800 doctors, general practitioners and specialists. It also was sent to the deans of medical and dental colleges. The booklet and the covering press release went to a press distribution of 15,000. Included were editors of daily and weekly newspapers, consumer magazines, veterans magazines and medical and dental journals, news syndicate managers, business editors, editorial writers, science writers, radio and TV commentators, news columnists and members of Congress.

Several days in advance of the release date every doctor and publisher who had given permission for quotes in the booklet received copies with a letter thanking them for their courtesy. One of these doctors, Edouard D. Gagnon, M.D., M.S., F.R.C.S., replied as follows: "... A perusal of this report and especially of the paragraph that concerns me has impressed me as being a non-biased statement of facts. ..."

One week after the press mailing a letter, over the signature of the Chairman, O. Parker McCormas, went to 114 key publishers and media heads calling their attention to the booklet. Following are several typical replies to the Chairman's letter:

"... I have read it with interest and have had it read by the heads of our Radio and Television News Departments as well as the head of the ABC Continuity Acceptance Department." - Robert E. Kintner, President, American Broadcasting Company

"... I have been a cigarette smoker for some forty-five years and I am still a pretty healthy specimen - despite the fact that I have had to listen to a lot of scare talk about cigarette smoking. What I believe the general public needs and wants is more light and not so much heat." - Roger H. Ferger, President & Publisher, The Cincinnati Enquirer

"Many thanks for sending me a copy of 'A Scientific Perspective on the Cigarette Controversy.' I shall look forward to future material as it is issued." - Roger Dakin, Editor, Collier's

"Thank you on behalf of Mr. Robert H. Reed, our editor, for your letter of April 14 and for the brochure titled 'A Scientific Perspective on the Cigarette Controversy' which accompanied it. We know only too well of the many unproven charges that have been made against the use of cigarettes. We shall, therefore, read this brochure with a great deal of interest." - J. T. Bingham, Associate Editor, Country Gentleman

"This will acknowledge your letter of April 14 with its enclosures, which I am sharing with my associates." - Arthur Hays Sulzberger, Publisher, The New York Times

PUBLICITY PLACEMENT

The Publicity Department of Hill & Knowlton, Inc. sent the booklet and release a week in advance of release to the news magazines. Several days in advance, ' press, network, wire services and columnist contacts were alerted by phone and in person. The booklet was hand delivered to newspaper desks and tobacco trade publications in the New York area. Hill & Knowlton, Inc. field offices in Los Angeles, Chicago, Cleveland, Pittsburgh and Washington, D.C. alerted local press, radio and TV to the story. Our Los Angeles field office made special placement to dailies, radio and TV stations in West Coast states.

PUBLICITY RESULTS

Substantial stories of several hundred words each were used by Associated Press, United Press, International News Service and Dow-Jones wires.

All New York dailies, Business Week, Newsweek, Printer's Ink, Advertising Age, and Editor & Publisher carried stories. At this writing, Time is planning a story in its next issue. The Sunday N.Y. Daily News (circulation 3,800,000) gave feature treatment to the booklet on their editorial page, devoting the major part of the page to comment and a cartoon.

AP radio news teletype sent the story to approximately 1,400 radio stations. Henry Gladstone did a piece on it for his Mutual syndicated business news program. Max Roby also used it on his KNX (Los Angeles) CBS Pacific Coast news program.

The story was carried by hundreds of papers and radio stations throughout the country. The Washington, D.C. Evening Star, the Cleveland News and the Chicago American carried special staff-written stories developed with the help of Hill & Knowlton, Inc. field offices.

Because clipping services are always several weeks behind, only a representative sampling can be shown with this report. Photostats of some of the news stories and editorials are attached.

Hill & Knowlton, Inc.

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attn.

Exhibit 7

HILL AND KNOWLTON, INC.

PUBLIC RELATIONS REPORT
AND RECOMMENDATIONS FOR
TOBACCO INDUSTRY RESEARCH COMMITTEE

6/21/54

(As discussed and approved on June 10 by a group of Public Relations people representing a number of Company members of the Tobacco Industry Research Committee. This group meets at intervals with Public Relations Counsel, to discuss TIRC Public Relations problems.)

Early in the life of the Tobacco Industry Research Committee, it was accepted as a basic principle that every effort should be made to avoid stimulating more adverse publicity and controversy on the subject of tobacco and health.

That principle has been and will continue to be carefully adhered to in the work carried on for the Committee. Nevertheless attacks on the industry recurrently stimulated by various individuals and groups antagonistic to tobacco, have been increasing, and some elements of the press are continuing to feature unfavorable aspects of any medical report bearing on tobacco.

On its part, the Committee properly has refrained from engaging in any direct controversy with the industry's critics. It has stood upon the basic statement of January 4 and upon the symposium of views of 36 scientists issued by the Committee in booklet form in April. Both of these statements received wide and favorable comment in the press.

In public relations recommendations submitted to the Main Committee in January, it was contemplated that a basis for an affirmative program of public information would be provided when the Scientific Advisory Board and Scientific Director had been selected and were at work, and when various preliminary editorial research projects were well under way. These things have been accomplished and the Committee now has the basis needed for carrying on a long-range plan of public relations activities aimed at establishing the TIRC in the public mind as a constructive force in scientific research. These activities will endeavor to keep the following facts before the Public:

1. That there is no proof that smoking is a cause of lung cancer;
2. That an impartial and independent Board of scientists, doctors and educators is advising the TIRC, as a public service, on all aspects of tobacco use and health;
3. That the TIRC is determined, through a long-range program, to make every possible effort to help get the facts through laboratory and statistical research;
4. That initial funds for research have been appropriated and more will be provided as warranted to help in getting the answers by scientific means;
5. That all the laboratory research recommended by the Advisory Board and financed by the TIRC will be carried on by recognized and independent laboratories, institutions and hospitals.

Report of Activities

As background for the recommendations which follow, certain active and continuing projects are briefly summarized:

Press Conference - First formal announcement of the appointment of Dr. Clarence Cook Little as Director of Research was made at a Press Conference, June 15, in New York City. A transcript of the conference has been sent to all TIRC members. Press, radio and television coverage was extensive.

TIRC as a Source of Information - Committee headquarters is steadily gaining recognition as a source of authoritative information on the subject of tobacco and health. The result is that news and magazine writers, columnists and commentators are turning to the Committee and its public relations counsel more and more for information. This will increase as the Advisory Board gets into action and more material is released.

As part of this service, bibliographic files are being developed for two purposes, (a) public relations reference; and (b) technical reference.

Clippings have been sifted for significant stories and ten publicity reports have been made to the TIRC.

Misstatements Corrected - Reports and statements appearing in the press, radio, television and newsreels are carefully monitored. Whenever misstatements are made steps are taken to correct the record. This has been done by personal contact and letters to the editor.

Coverage of Medical Meetings - With the cooperation of the AMA, the American Cancer Society, the New York Medical Society and industry people, close check is kept on medical meetings. A calendar of coming events having to do with tobacco and health is being maintained. The important ones are personally covered through New York staff or field offices and reports are being sent to the TIRC, its Scientific Advisory Board and Industry Technical Committee. Where possible, abstracts or texts of important papers are obtained for TIRC distribution.

Foreign Surveys - As proposed in the January 15 program, and approved by the Main Committee, surveys on the cigarette controversy have been conducted in European countries. Reports have been made on Switzerland, Belgium and the Netherlands, and detailed reports are in preparation on France and England.

Hill and Knowlton, Inc. overseas associates will continue to watch developments in these countries, particularly in Great Britain, where the government has taken an official position.

Correspondence and Callers - A large volume of public relations correspondence, which at times has topped over 100 letters a week, continues from lay press, trade press and the industry. Individual letters have been sent to a large number of doctors who wrote detailed comments on the "Scientific Perspective" booklet. Personal and phone calls of the same type are increasing.

In keeping with the objectives outlined on page one of this memorandum, the following recommendations are presented:

Reserve Fund - It is suggested that when the present fund of $500,000 for research is exhausted, or before, the Committee give consideration to setting up a substantially larger reserve fund for research over a period of two or three years. This will keep before the public a more accurate view of the magnitude of the job the industry has undertaken, and the sincerity of its purpose.

Releases - As developments warrant, and subject to approval of the Scientific Advisory Board, information on the work of the Board should be released to the public. Three such announcements have been made. As grants are made the essential facts of each should be released to the press. It seems probable that the Advisory Board will come forth with some new and intriguing ideas for fields of research. Dr. Little would be the logical spokesman for the Board in connection with such reports or any other statements to be made to the press, on the air, or before groups. Various opportunities for television appearances for Dr. Little will be explored.

Results of medical statistical research to be authorized by the TIRC should provide valuable information bearing upon tobacco use and health. It should be in order, subject to clearance in each case with the TIRC, to release some of this information to the press.

Science Writers Tour - As soon as enough grants are operating, a tour of some of the most significant research projects should be arranged for science writers. This would be similar to the project conducted by the American Cancer Society in April, when `O some top science writers were taken on a tour of the principal laboratories engaged in cancer research. Much good publicity resulted for the Cancer Society and its funds drive.

Background Memo and Booklet on TIRC and its Advisory Board - A brief editorial memo giving the facts about TIRC and its medical board is proposed as a follow-up to the press conference. This would be distributed to special press such as science writers, medical press and organizations; also to columnists, editorial writers and Sunday editors.

The material in this editorial memo could be developed into a dignified and effective booklet for wider public distribution to doctors, etc., as a follow-up to the "Scientific Perspective" booklet which was issued in April.

Editorial Contact Project - A program of informal contacts is being developed to enable Dr. Little to better inform important elements of the publishing field, and scientific and editorial writers, regarding the constructive aims and policies of the Tobacco Industry Research Committee and its Scientific Advisory Board. This activity will be centered in the important publishing center of New York.

In addition, public relations staff members should visit publishers, editorial writers and commentators in other principal cities.

Editorial Research - Continued emphasis should be given to editorial research. In the January 15 program, two lines of inquiry were suggested: (a) smoking habits of long-lived distinguished public leaders; and (b) human ills erroneously attributed to tobacco over the centuries. The second subject has been found more marketable and has received the placement emphasis thus far.

In addition, research should be carried forth on (c) current scientific opinion holding that no case has been proved against tobacco; (d) the many theories about cancer causes; and (e) the psychology of how the public is carried away by over-simplified reading of scientific experiments.

All the material resulting from this research would be made available to interested writers for magazines, newspapers, columns, radio and television. None of this would be for sponsorship or release by TIRC.

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Exhibit 8

T. V. Bertnett

August 17, 1954

Carl Thompson

Report through July 31

The attached report contains material that, as you will see, should be considered highly confidential and receive the minimum of circulation. However, you may want some of the other principals of the Tobacco Industry Research Committee to see or have a copy. Should you desire to make copies available to a few, it is suggested that you append a note to the front of the report to this effect:

"The attached report is highly confidential. It is requested that you retain it only for your personal consideration and for that of your immediate associates; also that no additional copies be made and that this copy not be placed in files."

When I assumed the chairmanship of the Tobacco Industry Research Committee, I asked for a detailed report from public relations counsel in order that I could be fully informed on the public relations and information program to date.

As I read it, it occurred to me there would be merit in bringing the report to your attention so that you could gain a closer acquaintanceship with this extensive program. I am sure that you will agree with my opinion this is a highly confidential report.

cc:

Mr.
Mr.

Mr. Hill
Gose
Hoyt

CONFIDENTIAL

TO: T. V. Hartnett, Chairman
Tobacco Industry Research Committee

FROM: Hill and Knowlton, Inc.

SUBJECT: Report of Activities through July 31, 1954

SUMMARY OF ACTIVITIES

The functions of public relations counsel have been threefold: (1) Over-all policy guidance and programming; (2) administration of Committee affairs; and (3) public and press relations and contacts. Since these functions frequently overlap, there can be no clear-cut delineation of activities into these three categories. In the first section of this report, "Summary and Background," the historical approach is taken. In the second section, "Other Public Relations Activities," a topical presentation is used.

SUMMARY AND BACKGROUND

In mid-December, 1953, executives of leading tobacco companies decided some kind of joint action was imperative in the face of widely publicized attacks alleging a link between cigarette smoking and lung cancer. Representatives of Hill and Knowlton, Inc., were invited to meet with these executives for consultation on ways and means of dealing with the problem.

At this first meeting, it was agreed that the wisest course of action would be for the industry to find out, through objective research, what truth there was, if any, in the charges being made against it. Mr. Hill stated it would be a serious public relations mistake for the industry to make any move that could cause it to be accused of disregard of people's health and under no circumstances could the industry afford to engage in direct controversy with its detractors. With the acceptance of these principles, Hill and Knowlton, Inc. was asked to recommend a program to implement them.

After two weeks of intensive study of the problem, public relations counsel developed a step-by-step program which was discussed at a meeting with a small group of public relations representatives of a number of tobacco companies. Valuable suggestions were made at this meeting, and the program was put into final shape and submitted to the principals at another meeting the last week of December.

Taking into consideration court ruling inhibiting the industry from ordinary trade association activities, the program recommended:

1. Formation of an industry group to be known as the Tobacco Industry Research Committee, dedicated to sponsoring and financing research into all phases of tobacco use and health.
2. Establishment of a Scientific Advisory Board, to be composed of distinguished research scientists and educators, and a Scientific Director, to guide the research objectives.
3. Undertaking of continuous editorial research into relevant scientific, statistical and medical material, past and current, for an effective information program.
4. Keeping the public informed regarding the Committee's activities. As a first step, a newspaper advertisement outlining the industry's plans was proposed, copy for which was submitted.

The program and the public statement advertisement were approved. The agreed-upon approach was to sponsor genuinely objective research and to bring to public attention the fact that there is now no conclusive proof that cigarette smoking is a cause of lung cancer or other serious problems of human health.

On January 4, the advertisement and news announcement appeared and the Tobacco Industry Research Committee was in being, with Paul M. Hahn as Chairman for the first three months.

Since the Committee had no headquarters and no staff, Hill and Knowlton, Inc. was asked to provide a working staff and temporary office space. As a first organizational step, public relations counsel assigned one of its experienced executives, W. T. Hoyt, to serve as account executive and handle as one of his functions the duties of executive secretary for the Tobacco Industry Research Committee.

Selection of Scientific Advisors

The task of selecting a Scientific Director prior to getting a Scientific Advisory Board proved difficult, and Chairman Hahn decided to reverse the order and select the Board.

Public relations counsel provided assistance in selecting and inviting a group of seven scientists, all of whom agreed to serve, and the first meeting of the Board was held on April 26.

On a number of occasions, from the start of the Tobacco Industry Research Committee early in the year, when his name was put forward by Mr. Hill, Dr. Clarence Cook Little was proposed to the Committee as excellent possibility for Scientific Director. When Dr. Little accepted a place on the Advisory Board, these recommendations were renewed to O. Parker McCoMas, who had become Chairman of the Tobacco Industry Research Committee, and various members of the Board. He was unanimously requested by the members to serve as Chairman and to consider becoming Scientific Director. On June 15, Dr. Little's acceptance was formally announced.

Dr. Little as Scientific Director

With a highly-respected and qualified scientist now in a position to speak for the Committee on its research problems, it became possible to meet more of the public relations problems facing the Committee.

For example, through Dr. Little's full cooperation in press conference arrangements that included photographers, radio, television and scientific writers, it was possible to achieve wide coverage of the purposes and philosophy behind the industry's research efforts.

After the Hammond-Horn report was delivered at San Francisco, Dr. Little was asked to dictate a statement by telephone from Bar Harbor which was put into shape for a press release. After clearance with the Scientific Advisory Board, this was issued to the press and widely used, resulting in tempering some of the hysteria caused by the Hammond-Horn report.

Dr. Little also approved an announcement of the outline of research adopted by the Scientific Advisory Board. Dr. Little's skeleton outline was developed into a full statement for general release to press and radio, with resultant wide and favorable attention.

Reaction of the press to such steps has been generally good, as exemplified in a column by Waldemar Kaempffert of The New York Times, dean of the country's scientific writers:

> "The case for and against tobacco consumption as a cause of cancer may be settled by the Tobacco Industry's Research Committee of which Dr. C. C. Little, former director of the American Cancer Society, is head. Many will argue that an impartial investigation can hardly be expected from a body of experts paid by the tobacco industry. Dr. Little is an eminent geneticist, a type of scientist who has the courage to face facts and to state them."

Because of his scientific approach, Dr. Little correctly feels that the industry must make no controversial statement on scientific matters unless fully supported by facts and approved by the Scientific Advisory Board.

Mr. Hartnett as Full-Time Chairman

Final step in the formal organization of the Tobacco Industry Research

Committee was the selection of Timothy V. Hartnett, retiring president of Brown and Williamson Tobacco Corporation, as full-time chairman, rather than to continue rotating the chairmanship. He assumed his duties on July 1, with appropriate public announcement.

Throughout the formative period, Chairmans Hahn and McConnas provided valuable leadership in developing both the organizational and public relations aspects of the Committee's work. Mr. Hoyt, with staff assistance, handled liaison, agendas, organizational plans, business affairs, reports, and materials for meetings of the Tobacco Industry Research Committee, the Scientific Advisory Board, and the Industry Technical Committee, in addition to developing operating procedures for the research program and carrying on continuing contacts with the Committee and Advisory Board members.

Periodic meetings are held with public relations representatives of the various companies. Worthwhile suggestions have come from members of this group, both at the meetings and in the interim.

OTHER PUBLIC RELATIONS ACTIVITIES

The information work of public relations counsel was carried on and developed throughout the formative period of the Committee. It includes several categories of activities which will be described in detail.

I. TIRC As An Information Source

A continuing important function is to build up the TIRC as a reliable and authoritative source of facts relating to the tobacco and health problem. That this is being done is indicated by the growing number of inquiries from writers and editors of various publications, newspapers, press services and broadcasting companies.

As a part of this work, the building and maintaining of a TIRC library of basic informational material is in progress. Present materials include:

1. A cross indexed card file on medical and scientific papers regarding smoking and health that are noted by the N. Y. Academy of Medicine in some 2,500 medical journals published throughout the world. Most pertinent material is obtained in full.
2. Basic books dealing with tobacco, its history, and other relevant technical or general volumes.
3. Special files of all pertinent press clippings.
4. A cross indexed card file on medical opinions regarding the cigarette controversy as noted in press, radio and other popular media is compiled from the clippings.
5. Full texts of speeches, announcements, panel discussions, and similar material which are germane and available.
6. Data relating to other related phases of smoking and health, both here and in foreign countries, obtained from established sources. This includes published material from U. S. Department of Health, Education and Welfare, Bureau of Internal Revenue, Department of Agriculture, Food and Agricultural Organization, the Tobacco Merchants Association and the U. N.
7. Curriculum vitae of Scientific Advisory Board members is maintained on file, as well as some information about their scientific work.

II. General News Releases

Eleven general news stories have been distributed since the formation of the Committee. In each instance, direct personal contact was made with major news outlets in the press, radio and magazine fields, through staff

members in New York and field offices. An indication of the results has been included in the photostatic news summaries that have been sent regularly to Committee members.

The releases were:

1. Announcement of the formation of the Committee, January 4, 1954.
2. Abstract of Dr. Rosenblatt's paper, March 17, 1954.
3. Announcement of publication of "Scientific Perspective," April 14, 1954.
4. Selection of Scientific Advisory Board, April 27, 1954.
5. Research Projects invited for consideration by Scientific Advisory Board, May 18, 1954.
6. Appointment of Dr. Little as Scientific Director of the Tobacco Industry Research Committee and Chairman of the Scientific Advisory Board, June 15, 1954.
7. Dr. Little's statement regarding the Hammond-Horn Report, June 22, 1954.
8. Mr. Hartnett appointed Chairman of the Tobacco Industry Research Committee, July 1, 1954.
9. Dr. E. B. Wilson becomes a member of Scientific Advisory Board, July 20, 1954.
10. Dr. Hueper's talk at Sao Paulo distributed with "Highlights," July 26, 1954.
11. Dr. Little announces scope of research program, July 28, 1954.

Each press announcement is prepared and distributed individually, according to the type of story. A case history of some of the steps taken on one release is that of Dr. Hueper's talk at Sao Paulo, Brazil:

1. Advance checking on the Sixth International Cancer Congress revealed that Dr. Hueper of the National Cancer Institute was scheduled to talk on "Environmental Cancer of the Lung." (Other information, of course, was also obtained and followed up.)
2. The Hill and Knowlton, Inc., Washington office, requested to follow up on this information, obtained from Dr. Hueper an advance copy of his talk and sent it to New York.
3. Study of the paper showed it contained newsworthy material concerning lung cancer and particularly concerning the lack of a proven link between lung cancer and smoking.
4. Further inquiry in Washington brought out that no press distribution of the talk was contemplated either by Dr. Hueper or the National Cancer Institute. In view of this, permission from Dr. Hueper was obtained to distribute copies of his talk to the press, on his strict condition that this be done only after it was certain that he had actually delivered it -- placing it in the public domain.
5. Reproduction of the 17-page paper, of two pages of highlights, and of a covering note to editors from Hill and Knowlton, Inc., and all preparations for distribution were made in advance of the talk.
6. Special liaison with representatives in Sao Paulo was established to give word of Dr. Hueper's delivery as quickly as possible, so as to enable distribution of the talk while it was still newsworthy. However, due to postponement in Dr. Hueper's presentation, this notification did not arrive until after 2 o'clock Monday afternoon -- quite late to begin press distribution.
7. Personal delivery of the Hueper release was made to important newspapers and services as well as distribution to science writers, editorial writers and feature writers. Evidence of use of the material

is still being observed. (For example, "Science in Review," page E-7, New York Times, Sunday, August 1; INS Sunday column for August 8; U. S. News and World Report, August 6, page 85.)

8. Although many of the writers covering the Sao Paulo meeting failed to mention the Hueper talk in their dispatches, it is significant that, as a result of the distribution in the U.S.A., stories questioning a link between smoking and cancer were given wide attention, both in headlines and stories. In some press accounts, the Hueper story took precedence over the reports of Drs. Hammond and Wynder, even though the latter were made available to the press in advance of their delivery on a hold-for-release basis.

III. Special Assistance to Press, Radio, Magazines and Others

This category might include many more items than those listed since there have been numerous telephone calls and personal contacts made on which the ultimate results are not yet known.

Following are some examples of such assistance:

1. Considerable source material was read and digested to provide facts for a column written by Hal Boyle, distributed nation-wide by the Associated Press. (Note: Many of the basic facts also are incorporated in material given to other writers.)

2. Special personal contacts are being made regularly with Time, Newsweek, U. S. News and World Report, and Business Week editors to encourage use of TIRC material.

3. Through personal contacts, advance information was obtained that a prominent magazine intended to report a growing lack of interest in the TIRC program on the part of participating companies. This ref-

erence was removed from the story when the facts were brought before the magazine editors.

4. By personal contact, advance knowledge was obtained of a story on smoking by Bob Considine for Cosmopolitan Magazine. Information was supplied resulting in seven revisions and five qualifying additions to the story which was already in type.

5. Considerable information and assistance was provided Donald G. Cooley in the preparation for his story in True Magazine. This entailed conferences with the author to work on factual revisions.

6. Further research and assembling of material and personal conferences have been extended Mr. Cooley to provide him requested aid in his writing of a 48-page, low-priced book for newsstand sales and angled at the idea "You don't have to give up smoking." Fawcett Publications is issuing the book entitled "Smoke Without Fear," in late August and early September.

7. Personal discussions with editorial writers and the supplying of material preceded the appearance of several positive editorials in the New York Daily News.

8. Several other editorials which have appeared in newspapers throughout the country were the result of information provided by mail or through direct personal contacts by branch office staff members of Hill and Knowlton, Inc. Editorials in the influential Washington papers are an example.

9. Two editorials widely used in "home town" dailies and weeklies throughout the country were prepared for and then distributed by the U. S. Press Association. These were "The Same Old Culprit" and "Truth Makes a Slow Crop." Over 100 clippings of these have already been received.

10. Through personal contacts radio and TV newsmen and commentators receive frequent information concerning TIRC activities. Some of the results of such efforts show in the press-radio-TV reports. For example, Dr. Little's press conference was reported on film on: NBC-TV network, "Today"; NBC-TV and CBS-TV syndicated newsreels, UP Movietone News; and MGM Telenews, both of which go to some 80 TV stations. Radio uses included Lyle Van, WOR; Frank Edwards, MBS network; the Yankee Network; KHJ, Los Angeles and the regional MBS West Coast network; CKLW, Windsor, Ont.; KNX, Los Angeles; KABC, Los Angeles, and the regional ABC West Coast network. At other times, many programs which indicated an interest in presenting TIRC facts sought an interview or appearance by a TIRC spokesman but these requests could not be filled.

11. One negatively-aimed program (WNBT) which was being scheduled on the cigarette controversy was postponed after discussion of TIRC facts.

12. Another TV program (ABC-TV, Martin Agronsky), which did deal with the cigarette controversy, ended on a favorable note after conferences with producers and presentation of facts.

13. A special radio script for a Louisville, Ky. radio interview with T. V. Hartnett was prepared and used.

14. Conferences were held with Dwight Macdonald regarding article he was preparing for The New Yorker. Macdonald was doing research on an article that was to be a blast at the tobacco industry. "Special data" he wanted were "accurate figures" regarding the number of scientists who were unconvinced by charges against smoking. A list was prepared of over 100 eminent cancer experts, each of whom had

stated since 1948 that, in his (or her) opinion, no conclusive evidence has been established linking tobacco and lung cancer. Other information also was supplied. No article by Macdonald on this issue has yet appeared.

15. Assistance was provided to the New York Times for a Sunday Magazine piece which appeared on Sunday, July 4, on "Why People Smoke," which discussed some of the now-abandoned old charges against cigarettes.

16. The Louisville Courier-Journal story on the Kentucky Heart Association statement was obtained in New York from Louisville by telephone and supplied to the news services, editorial writers and columnists. The story was carried by INS, the New York Journal-American and other papers.

17. Early in the public relations program, an informal survey of magazines, features and syndicates was undertaken to see what, if any, articles were planned on the smoking controversy, and to follow up in any way possible. Twenty magazines of nation-wide circulation were checked and it was found five magazines were working on pieces and contact was established with authors and editors. Such regular checking continues as standard practice, requiring numerous contacts weekly.

18. Conferences were held with and materials supplied to Hertha Striker of Coronet Magazine for possible article.

19. Special Fact Sheet on TIRC was supplied to Dr. Charles S. Cameron prior to his talk before the National Press Club in Washington in June. The material was used in his question-and-answer period. At the same time, multiple copies of True Magazine with Don Cooley's

smoking article were made available at the Press Club for pick-up following the Cameron appearance.

20. Special conferences are held with AP, UP and INS science writers. These have been helpful in obtaining guidance on attitudes of writers, in learning best sources of information from them, and in learning best methods of supplying information to them.

21. Often news releases become available late in the day, when most "inside" newspaper matter is set. Personal outlets with wire services, including telephoning texts of releases, are necessary to get coverage. Frequently, this means individualized services, such as the handling of a story on Dr. Little's press conference to International News Service, which was unable to send a man to cover the conference.

22. Conversations were held to supply information to Robert Heilbroner whose balanced piece on the cigarette controversy appeared in the June issue of Today's Woman.

23. Available material was supplied to Sheldon Binn of the New York World-Telegram & Sun for his January series in the Scripps-Howard papers and for his article in Real Magazine issue of May.

24. Personal conferences were held with writers for the N. Y. Post, which ran a well-balanced series on the cigarette controversy.

IV. Editorial Research and Materials

Public information for the TIRC has been handicapped by the time required to pull together an adequate body of organized factual material. This applies not only to the current controversy in the news, but to facts relating to many other aspects of smoking, suitable for suggestions for use by news writers, columnists, magazine writers, and others.

(The program approved by the industry in December contained a recommendation for the development of such editorial research material and this research is in process, with much of the material now in hand. One aspect of this research bears on public attitudes, but is not directly concerned with either medical or statistical research. Therefore, it is being done by Hill and Knowlton, Inc. research staff members, and by outside science writers. The purpose is to have a supply of colorful and interesting information on hand for writers.)

Some of the scientific and editorial materials already distributed or still in preparation are:

1. "A Scientific Perspective on the Cigarette Controversy." This was undertaken before a Scientific Advisory Board or a Scientific Director had been named. It was held necessary and urgently timely to present to leaders of public opinion the fact that there was no unanimity among scientists regarding the charges against cigarettes. Quotations from some three dozen research and medical authorities were assembled from authoritative sources in this country and abroad. The Law Committee ruled it would be necessary to get a written permission for each quotation. This involved getting clearance, in most cases, from the publications as well as from the individual scientists. Some weeks were required to cover this ground, but on April 14, 1954 the booklet came off the press and copies were distributed to doctors, scientists, editors, and many others. The publication has since been used as source material for writers on the subject. It was widely publicized and resulted in many favorable editorials, including a lengthy one in the June, 1954 issue of the Western Journal of Surgery, Obstetrics and Gynecology.

2. A special packet of timely background information was compiled following the Hammond-Horn Report in San Francisco and hand-distributed or mailed to editors throughout the country. Included in this packet were: Statements by Dr. Little, Dr. Cameron and the American College of Chest Physicians; excerpts from Dr. Weller's report and Dr. McCormick's statement and an information summary on TIRC.
3. A basic information folder has been assembled to include all important material on TIRC. This is intended for hand and mail distribution on an individual basis to by-line writers on the subject, new contacts in the various media, and others who are planning articles. Included at this point are: The original TIRC advertisement, a statement concerning origin and purpose of the TIRC, a "Scientific Perspective," the column by Hal Boyle, the release on Dr. Little's appointment, a condensation of Dr. Little's June 15th press conference of the TIRC, press background material, historical tobacco facts, Dr. Hueper's paper, and the release describing the scope of research interests.
4. In final stages of preparation is a Background Memorandum on the Tobacco Industry Research Committee, designed to set forth succinctly the organization, research policy, scope and purposes of the group. This will supplement and become a part of the Basic Information folder and will also be available to answer inquiries about the Committee.
5. "Editorial Comment on Tobacco and Health" is nearing completion. (Due to be distributed on or about August 20.) This is a 20-page compilation of newspaper editorials, by-lined articles, and columns relating to the smoking and health controversy that have appeared

throughout the country. Copies of this booklet will be distributed to newspaper editors and writers to provide information and stimulate positive action on future editorial writing. Material was carefully screened to select articles which were well-balanced but at the same time would not unnecessarily antagonize. Permission to reprint was obtained from each publisher, syndicate or author.

V. Informational Reports to TIRC

A continuing effort is made to keep members of the TIRC and related committees informed of current or anticipated events. This function entails the reading and culling of hundreds of published clippings monthly; of monitoring radio programs; of mail and personal contacts with sources of news or developments in publications and in medical and research organizations; and then determining what is of sufficient importance for special communications to the TIRC.

1. Regular reports are being made to TIRC groups on editorial, news, feature, radio and magazine attention given to the subject. These comprise selected pieces that are representative of published material. Special mailings of such compilations are made from time to time on specific articles or events.
2. Other informational mailings to the Committee have included:
   a. Advance notice on Reader's Digest article that appeared in the July issue - May 3, 1954.
   b. Report on the Industrial Health Conference, Chicago.
   c. Report on the article, "The Harmful Effects of Tobacco," appearing in the magazine, "New York Medicine."
   d. Report on the American Association for Thoracic Surgery Conference in Montreal.

e. Report on the National Tuberculosis Association meeting in Atlantic City.

f. Transcript of the Dr. Charles S. Cameron talk at the National Press Club.

g. Report on the American Association for Cancer Research session at Atlantic City.

h. Preliminary report on the American Medical Association Convention in San Francisco.

i. Excerpts from the Annual Report of the British Empire Cancer Campaign.

j. Advance report on plans for the International Cancer Congress in Sao Paulo.

3. Much reporting is done that does not go out in mailings. For example, leading life insurance companies were checked as to their plans to adjust premium rates for smokers, as had been reported in some press accounts. It was found no such move was contemplated and this information was passed along informally to interested committee members and press contacts.

VI. General Contacts -- New and Old

Personal contacts are advantageous not only in disseminating and gathering information but for enlisting support and advice on problems. Relationships established with scientists in connection with the "Scientific Perspective," for example, helped lead to selection of several members of the Scientific Advisory Board.

1. Personal liaison has been established in such cancer, research, and medical organizations and associations as the American Medical Association, American College of Chest Physicians, American Cancer Society, Sloan-Kettering Foundation, New York University School of

Industrial Medicine, National Cancer Institute, International Cancer Congress' Cancer Prevention Committee, as well as with individual doctors and scientists. These continue to make possible obtaining advance information or papers concerning research being done in this and related fields.

2. Personal contacts with selected science writers, editorial writers, columnists, publishers, magazine writers and editors are being broadened, in relation to TIRC activities. This is in addition to normal press relations activities or handling of specific requests and projects.

3. Mailing lists, another important form of direct contact, are tailored for maximum effectiveness. In addition to general paper and wire service lists, special categories are maintained for the Association of Science Writers, medical journals, trade associations and trade publications, by-line writers who have shown an interest in the subject, selected free-lance writers, editorial writers and columnists, medical columnists, and tobacco country newspapers. Regular revision, additions and deletions are made.

4. Several movies have been screened. "Alcohol and Tobacco: What They Do to Our Bodies" (Coronet Films) appeared to present a real problem, but this has been withdrawn. "One in 20,000" featuring Dr. Ochsner was screened and several approaches have been made to sell TIRC full rights to the film for $250,000 (no doubt a bargaining figure) but these overtures were definitely and emphatically rejected. This film still apparently has not been made available for distribution. A Fox Movietone newsreel featuring Dr. Ochsner was screened with a

recommendation of no action. A proposed anti-tobacco film, "Slow Suicide," was investigated; this project had been abandoned at last report.

VII. Meetings -- Calendar, Coverage and Reports

1. A calendar of state, national and international medical and scientific meetings which may bear upon the subject is kept up to date. Information contained in these lists include the location of the meeting, its sponsorship and the persons in charge. Agendas are obtained by correspondence and/or personal contact. Whenever desirable and available, abstracts of appropriate papers to be presented are obtained in advance. (See discussion of Dr. Hueper's paper under "I".)

2. Individual coverage of medical and scientific meetings such as the AMA meeting in San Francisco have resulted in first-hand knowledge of the theories, methods, and personalities of those involved in the research on tobacco and smoking, in an awareness of reactions to and an understanding of the theses which may be expected to be advanced from various individuals in the future.

3. On-the-spot coverage of these meetings also makes possible securing for TIRC such items as the tape recording transcript of Dr. Hammond's presentation at the AMA meeting, the original press release and official statements on which newspaper accounts are based, transcripts of papers given and press conferences held, contact with the press representatives as well as scientific personnel. A representative at Sao Paulo, for instance, alerted U.S. newsmen to Dr. Shear's talk, although no copies of his paper were available. (See AP dispatch from Sao Paulo, Pueblo, Colo., Chieftain, July 27, 1954.)

VIII. Foreign Studies and Liaison

Upon approval by TIRC, Hill and Knowlton, Inc. asked its associates in England, France, Switzerland, Belgium and Holland to submit reports on the smoking controversy in their respective countries. Summaries of these reports, except the one from England, have been prepared and distributed to TIRC members. The British report is in course of preparation.

In March, Mr. Hill had a meeting in London with the heads of the tobacco industry of Great Britain, including Sir Robert Sinclair, and Messrs. Oppenheim and Partridge.

The work of the TIRC was explained to the British group, and certain suggestions from them regarding the "Compendium" were received and submitted to Chairman Hahn. Also, it was suggested to the British group that the Hill and Knowlton, Inc. English associate, Alan Campbell-Johnson, could if desired act as liaison through which the British industry could clear information regarding developments which it desired to communicate to TIRC. This arrangement was confirmed by Mr. Hartnett when he was in London later in the Spring.

A FORWARD LOOK

Although the industry has been bedeviled by sensational headlines generated often by publicity seeking researchers and a seeming revival of the anti-cigarette crusade, the trend is beginning to turn. In 1953, no voice was being raised in behalf of the industry. Press comment was almost entirely limited to a reflection of unproven theories which most people were accepting as proven facts. No balancing information was being made available.

The progress of the Tobacco Industry Research Committee's program is bringing greater acceptance of the industry's sincere efforts. The publicity accompanying each step taken so far by the Tobacco Industry Research Committee, particularly since the selection of the Scientific Director and the Scientific Advisory Board, has helped bring understanding that the charges against tobacco are not proven and are not joined in by a large body of scientific opinion. The bulk of editorial comment now appearing approves and, at times, applauds the action of the industry.

There are, however, many indications that the researchers and associations who have led the attacks against cigarettes are going to continue their efforts publicly and are even more anxious than ever to justify their position and put their case before the public. Recurrent publicity about such attacks can be expected and is anticipated.

It is not enough, of course, to be prepared to answer (or prepared not to answer) attacks when they come. It is necessary to continue building a broad base of public knowledge of the total story. Progress is being made along these lines:

1. Basic Public Approach. In all endeavors, continuous emphasis is placed on (a) informing the public of the

4. Special Editorial Material. Especially-written articles are being developed that can be used or adapted for use in various media receptive to or seeking material relating to the subject. These will not be limited to the cigarette controversy but will often deal with broader fields of research on cancer and other health questions. The purpose is to spread a wider understanding of all factors involved without directly encouraging continuing articles on just "The Controversy." To achieve this objective more quickly and effectively, the free lance services of qualified science writers are being used.

5. Congressional Information. A congressional information project is being developed, designed to better inform those members of Congress from leading tobacco-interest states whose constituents have a direct interest in the problem.

6. Publicity for Grants. The judicious use of information concerning the research grant program, just now getting started, will include immediately the announcement of grants as they are made as well as follow-ups as some of the research gets underway. Proper handling will be worked out in conjunction with the Scientific Advisory Board.

7. Special Editorial Services. Several projects are now underway to provide special material to writers, publishers and radio-TV producers for work they plan relating to the subject. Among those now in progress are Jack Ratcliff, for story idea in Cosmopolitan; Leonard Engel for tentative

(Page 22 is missing)

Harper's assignment; U. S. News and World Report for proposed interviews with Drs. Hueper and Shear of National Cancer Institute; Fred Friendly of the Edward R. Murrow show; United Features for a possible series on Dr. Hueper's work; Ernie Heyn of American Weekly; Wade Nichols of Redbook and Bluebook; Sumner Alhbum of Newspaper Enterprise Association; and Pete Arthur of Associated Press Features.

8. Review of Scientific Papers. Recent scientific papers are being reviewed in detail and findings summarized in order to supplement and improve the amount and quality of information that can be made available. This will be organized according to subject matter (i.e., "smoking machines and what is being done with them" and the like).

9. Continuing Projects. In conformance with the Public Relations Report and Recommendations approved on June 10, activities are going forward in broadening and intensifying press and public contacts; the search for and compilation of information, here and abroad; making full use of material that can be issued as general press releases; channeling background information where it will be most effectively used; encouraging writers and others to regard the Tobacco Industry Research Committee as a reliable font of basic information; keeping the Committee informed on all significant developments; exercising constant alertness for possible new attacks on the industry or support for the industry's approach to the problem; and constantly evaluating the progress and activities to assure maximum effectiveness and new approaches and action as developments warrant.

Exhibit 9

Hill Knowlton 329
F.: TIRC Con 1917

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BILL AND KNOWLTON, INC.

CONFIDENTIAL MEMORANDUM

SUBJECT: Tobacco Industry Research Committee Information Activities, August and September, 1954.

The following is a summary of recent major public relations projects for the Tobacco Industry Research Committee covering August through September. In addition, assistance was given to various news and feature writers in response to inquiries.

Conferences with Publishers

Conferences with several major publishing groups in New York City were planned and carried out for Dr. Clarence Cook Little, Scientific Director, and Timothy V. Hartnett, Chairman.

Sessions were held with the following:

New York Times: Arthur Hays Sulzberger, president and publisher; Charles Merz, editor; Turner Catledge, managing editor; Julius Ochs Adler, vice-president and general manager; Lester Markel, Sunday editor; Orvil E. Dryfoos, assistant to the publisher; Robert K. Plumb, science writer; Luther Huston, Washington Bureau and Dr. Matthew Rosenschein (an M.D. Like Mr. Dryfoos, he is a son-in-law of Mr. Sulzberger).

New York Herald Tribune: Mrs. Helen Rogers Reid, chairman of the board; Geoffrey Parsons, former chief editorial writer, now retired into a consulting capacity; Luke Carroll, news editor; Earl Ubell, science editor.

Scripps-Howard Newspapers: Jack Howard, president.

Hearst Consolidated Publications, Inc.: William Randolph Hearst, Jr., president and publisher; Richard E. Berlin, president of the Hearst Corporation (the magazine corporation); Glen Neville, editor, New York Daily Mirror; Frank Coniff, chief editorial writer, New York Journal American, and assistant to Mr. Hearst; Seymour Berkson, general manager, International News Service; Sam Day, managing editor, New York Journal American.

Luce Publications: Roy E. Larsen, president.

At each conference Dr. Little outlined the scientific approach being developed by him and the Scientific Advisory Board and made clear the freedom of action given the Board and research grantees. Mr. Hartnett explained the industry's long-range intention to support a research program devoted primarily to the public interest.

Each session resulted in interested questions and lengthy discussion, both of the industry's problem and of the scientific soundness of the Tobacco Industry Research Committee approach. Constructive suggestions were made

on the approach to the public information program. There was also expression on the part of the publisher-participants that the sessions had been most helpful in clarifying the Tobacco Industry Research Committee program.

Edward R. Murrow Television Show

Continued assistance has been given to the staff of the proposed "See It Now" program being developed for presentation later in the fall, the exact date not yet set.

A conference was held with Edward R. Murrow, Fred Friendly, his producer, and Arthur D. Morse, researcher and writer, at the Tobacco Industry Research Committee offices in the Empire State Building. Mr. Hartnett and Dr. Little were in attendance, in addition to representatives of Hill and Knowlton, Inc. At this conference Mr. Murrow made clear his intention to follow through on the program and indicated the only possibility of his discarding it would be the finding that the material collected was not suitable for telling a good story through the medium of television. The Murrow staff emphasized the intention to present a coldly objective program with every effort made to tell the story as it stands today, with special effort toward balanced perspective and concrete steps to show that the facts still are not established and must be sought by scientific means such as the research activities the Tobacco Industry Research Committee will support. Mr. Murrow was assured of continued cooperation from the Tobacco Industry Research Committee to the extent possible under the scope of the TIRC program.

In fulfillment of this assurance, Mr. Morse was assisted in visiting the Jackson Memorial Laboratory at Bar Harbor, and in interviewing Dr. Paul Kotin, University of Southern California, Los Angeles. Included also was the filming of a sequence of Dr. Kotin in his laboratory in California. Arrangements were also completed for the shooting of separate sequences with Dr. Little and Mr. Hartnett early in October.

Magazine Articles and Writers

In addition to routine contacts or conferences, the result of which are not yet certain, the following can be reported:

Investor's Reader: Personal conferences were held and material supplied to Miss Anne Holden, staff writer for the Investor's Reader, publication of Merrill Lynch, Pierce, Fenner & Beane. The article appeared in the September 8, issue and although primarily devoted to financial analysis of the companies, its references to the activities of the Tobacco Industry Research Committee were well balanced.

Harper's: An article being prepared by Leonard Engel for Harper's magazine was re-scheduled from the November to the December issue. Mr. Engel continued to use TIRC as a source of information and,

near the completion of his writing, was put in touch with Dr. Kotin, at Mr. Engel's request, for information concerning proved carcinogens in air pollutants. Engel's article will not be solely a defense against the cigarette attacks, but will attempt to analyze the charges in the light of the widely prevalent skepticism concerning the extent to which cigarette smoking can be implicated. On balance it should lend weight to the industry's contention that there is no proof of the charges and that there are many other factors that enter strongly into the increasing incidence of lung cancer.

Current Medical Digest: As a result of distribution by Hill and Knowlton, Inc. of Dr. W. C. Hueper's talk at Sao Paulo, a condensation appears as the lead article in the October issue of Current Medical Digest, which came off the press at the end of September. The Williams and Wilkins Company, Baltimore publishers of the magazine, says that the publication reaches the 123,000 doctors in the country under 65 years of ago who are in active practice.

Special conferences were also held with Jules Billard and W. C. Bryant, U.S. News and World Report; Art King, TV Age; Marguerite Clark, Newsweek; Lawrence Anderson, American Press.

Newspaper Writers

Washington Post: A feature story by Nate Haseltine using long excerpts from paper by Dr. Hueper, which was supplied him in personal contact through Hill and Knowlton, Inc., Washington office.

International News Service: The Sunday feature story distributed in mid-August by International News Service science writer Jack Geiger was developed primarily from the Hueper talk.

Associated Press: Through Pete Arthur, feature editor and Alton Blakeslee, science editor, material has been supplied for the basis of an Associated Press feature story, or series, on the development of the Tobacco Industry Research Committee. Two sessions with Dr. Little were set up for Mr. Blakeslee to get more background for the article. The piece awaits a news peg before being completed and sent out.

New York Post & Post-Hall Syndicate: At the request of Columnist Sylvia Porter, considerable material was rounded up and made available concerning Internal Revenue Service figures on cigarette manufacture and removals. Miss Porter was also referred to Harry S. Wootten for further industry information which she desired concerning cigarette sales outlook.

Science Writers

Personal contacts with science writers for general purposes as well as for specific assignments were expanded. Included in personal contacts were: Alton Blakeslee, Associated Press; Jack Geiger, International News

Service; Robert Plumb, New York Times; Earl Ubell, New York Herald Tribune; Roland Berg, Look Magazine; Marguerite Clark, Newsweek.

In addition, a number of writers were interviewd for research reports, looking toward possible magazine articles.

C. B. Colby, free lance popularizer of science, was retained for research and possible writing of article concerning all the hazards of modern life which people are cautioned against and leading to the conclusion that in spite of all the health scares, "You Still Live Longer."

Robert T. Miller, an experienced researcher, writer and public relations man, was assigned a research report on the wide range of things common today which are suspect as carcinogens. A tentative agreement was reached with another writer to popularize the technical Hueper paper but this has been postponed.

Special conference was held with Pat McGrady, science editor of the American Cancer Society, who has been critical of some of the material issued for the Tobacco Industry Research Committee, specifically the "Scientific Perspective" and Dr. Hueper's paper. Mr. McGrady was informed of the great precautions taken prior to the preparation and distribution of both of these. His objections were also checked informally with other science writers and there appears to be little agreement with Mr. McGrady's position that these materials should not have been issued.

Material Issued

An announcement of Dr. Julius Comroe's addition to the Scientific Advisory Board was released to the press on August 19.

Two other releases were prepared for and are awaiting clearance by Dr. Little and the Scientific Advisory Board. They deal with the statement of policy on research grants and a news announcement on the issuing of the first grants.

Three statements by Dr. Little that could be used in the event a press comment is needed were prepared and are being cleared with the Scientific Advisory Board.

The booklet "Editorial Comment on Tobacco and Health" was distributed widely to press and information leaders. Some strategic use of this material has already been noted, both in the press and on the radio or TV.

Mailing and Lists

A special mailing was made to selected papers in tobacco areas in 16 states. This included a letter informing the editors of material available concerning the Tobacco Industry Research Committee, a copy of the "Editorial Comment" booklet and the "Scientific Perspective." These same papers will be included in future distribution of releases and background material.

Special lists were also prepared on radio commentators throughout the country who have been noticed as devoting more than passing attention to the tobacco and health issue.

Hill and Knowlton, Inc.

10/7/54

Exhibit 10

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F: Budgets

HK 32

November 26, 1954

MEMORANDUM TO: Mr. Timothy V. Hartnett

FROM: John W. Hill

RE: Proposed Budget for 1955

Attached are budget estimates for operations of the Tobacco Industry Research Committee during the calendar year 1955. The budget for public information activities reflects the increased activities made necessary by growing press interest in the subject of tobacco and health as well as additional efforts to get the industry's case before the public.

The budget for staff operations provides for the use of all or part of the time of 26 different staff members of Hill and Knowlton, Inc. This compares with a total of 23 people, full or part-time, provided for in the Tobacco Industry Research Committee budget as revised on June 30, 1954.

The staff budget provides for one additional staff member to assist on science writing, editorial research and coverage of scientific and medical meetings. Informational assistance to other organizations interested in helping with the public education program is reflected in the budget for field offices and in increased provision for travel expenses.

The budget for Printing, Booklets, etc. is shown at $70,000. This covers three large-~~volume~~ quantity items, the first of them being a booklet describing the research program of the Tobacco Industry Research Committee. This would be published in quantities of 200,000 in order to cover all doctors, science writers, editors and editorial writers and to provide a quantity available for distribution at booths at medical and scientific meetings.

The Booklet budget also provides for a question-and-answer booklet, quantity 100,000, to be distributed to medical, scientific, editorial and other groups. This would cover the subject of tobacco and health more broadly, giving perspective on the present controversy.

The third item is provision for a wide mailing of at least one reprint of an important and helpful article such as the Leonard Engel piece in the December issue of HARPER'S Magazine, which is covered under the estimated expenses for 1954. The reprint to be mailed in 1955 has not yet been selected, of course.

In addition, you will note that there are additional recommended projects. The first item is $250,000 for one nation-wide advertisement reporting to the public at the end of TIRC's first year. The second provision is for two additional

cont'd

booklets and another mailing of a magazine reprint. This allocation of $57,000 would cover the preparation and mailing of an up-dated scientific perspective presenting some of the excellent medical and scientific information of a helpful nature which has become available in the past eight months, and a more limited booklet based on favorable editorial attention to tobacco and health. The reprint budget allocation would be used to give wider visibility to another article of specific value to TIRC's objectives.

I believe you are generally familiar with these details and other items of the budget as proposed. Please let us know if you need anything further from us.

Kind regards.

John W. Hill

jwhsw

HILL AND KNOWLTON, INC

Exhibit 11

HK30

CONFIDENTIAL

PUBLIC RELATIONS REPORT

to the
TOBACCO INDUSTRY RESEARCH COMMITTEE
April 28, 1955

The foundation which the Tobacco Industry Research Committee has been building is gaining strength in both breadth and depth. The progress of the scientific program developed by the Scientific Advisory Board is an essential and perveding force. The sound approach to the problem by the Scientific Advisory Board has encouraged other qualified scientists to speak out courageously in questioning those who would write off the lung cancer problem as a smoking problem.

Of necessity, efforts to bring the known facts before the public continue to be in the nature of an educational campaign -- slow, unsensational, factual. Neither the circumstances nor the available information lend themselves to the sensational treatment accorded the major indictments of tobacco use.

Factors Show Improved Position

Nevertheless, progress has been made. On the positive side, these factors stand out:

1. The first "big scare" continues on the wane. There is much general awareness of the big IF factors involved. In some instances, the accusers have gone to such extremes that their credibility is being questioned by their colleagues in their own profession.

2. The research program of the Tobacco Industry Research Committee has won wide acceptance in the scientific world as a sincere, valuable and scientific effort. This is due primarily to the stature of the men serving on the Scientific Advisory Board, the soundness of the research program developed, the caliber of research so far approved, and of the investigators receiving grants.

3. The status of the Tobacco Industry Research Committee itself has been enhanced by the freedom of action granted scientists, the increase to $1 million of research funds, and the obvious sincerity of approach to the problems. Both governmental and institutional groups in the field of health have shown recognition of the contribution the Tobacco Industry Research Committee is making.

4. There is greater and growing expression of the position that cigarettes do not and should not stand convicted. This is evident in both the scientific and lay communities. Suspicion is still widespread but the lynching party seems to have been called off, at least temporarily.

5. Treatment of the cigarette-health issue in public media continues to improve from the Tobacco Industry Research Committee point of view. Even adverse stories now tend to carry modifying statements. Positive stories are on the ascendency. They may not always be in the places we would like to see them and they may not always say the things we would like them to say. But at least they are now showing up and they do cast doubt on the cigarette attacks. A year ago attacks predominated and they were generally immoderate.

Issue Being Kept Alive

On the other side of the ledger, we have to face up to these situations:

1. The cigarette-health issue is still considered top news. This is often more apparent at a local level than in national news. While there is a growing tendency to emphasize the uncertainties and disputes in the issue, the end result is to keep the controversy constantly alive.

2. Medical, dental and other groups continue to schedule cigarette-health discussions, oftentimes for the apparent purpose of stimulating interest in their meetings.

3. Anti-tobacco crusaders continue to ride the health issue. Our clippings show continual local activities by the American Temperance Society, the Seventh Day Adventists, and similar groups scheduling lectures and movies dealing with the cigarette and health issue. Dr. Ochsner and Dr. Wynder continue to be the leading anti-tobacco crusaders of stature in the medical and scientific world.

4. While the American Cancer Society has tempered its emphasis on the lung cancer and smoking issue so far as its national fund drive publicity is concerned, it continues to play up smoking and lung cancer in its literature. Local groups also use the issue, particularly the Hammond-Horn findings, in their fund raising drives.

5. An increasing number of scientists and researchists are anxious to report on their works involving cigarettes. Of late, most of these have been anticipated and, when necessary, steps are taken to deal with the findings. These reports include studies on the relation of tobacco and heart as well as tobacco and lung cancer.

(Page 3 is missing)

5. A 6,000 word manuscript by John Pfeiffer, well-known science writer, has been prepared and is now in process of preparation for wide use. This discusses the "Fight Against Lung Cancer," with all elements placed in perspective. It is designed as the basis for a T.I.R.C. document and for other public distribution material, for articles and for policy statements.

6. Clearances are continuing for a possible brochure of news reports of doctors and scientists who question the cigarette link or express reservations about it. It is felt that publication should not be rushed, but the material is kept up-to-date for possible quick issuance.

7. Current scientific reports are screened as they appear for possible inclusion in a new scientific perspective, as well as for adding to scientific files for special reference and distribution.

8. Reprints of the PAGEANT article by Dr. William Rienhoff are being widely distributed to various media through the publishers of Pageant. A news notice summarizing the article was widely released by the magazine.

9. The article by Dr. Herbert Arkin appearing in the April issue of CURRENT MEDICAL DIGEST is being reprinted for broad distribution.

10. News releases on announcements of grants and increase of the research funds to $1 million were widely published. A special article concerning participation of the Medical College of South Carolina was prepared for and used by the CHARLESTON NEWS AND COURIER.

11. Information was supplied for the article "Phoney Cigarette Scare" in the March 23 issue of PEOPLE TODAY; for "A Psychologist on the Cigarette Scare" in the April issue of POPULAR MEDICINE, and for a piece scheduled for the August issue of ARGOSY magazine.

12. Information supplied to TV station KALB in Alexandria, La., was used April 17 when Dr. Ochsner appeared on a local program devoted to a review of his book. Reviews from CALIFORNIA MEDICINE and the AMERICAN PUBLIC HEALTH ASSOCIATION JOURNAL, as well as Dr. Rienhoff's article in PAGEANT, provided information for the rebuttal.

After considerable negotiation, recent permission was obtained to distribute to radio stations recordings of a panel discussion on the problems of aging, featuring three doctors, including Dr. Elmer Hess, president-elect of the American Medical Association, in which the question, "Does Smoking Shorten the Average Life?" was interestingly discussed.

13. The book, "Why Stop Smoking?" by Albert Ostrov has been officially published and first promotion started in Chicago last Friday. A special press release commenting on the book has been prepared by the publisher, E. P. Dutton for distribution to press and radio stations throughout the country. Most recent information is that the book has already gone into a second printing.

14. A proposed syndicated feature story devoted almost entirely to Dr. Wynder's opinions and research was checked by the editors for additional facts and information. This story is being held in abeyance pending possible development of a series.

15. The Public Affairs Committee pamphlet by Pat McGrady, science editor of the American Cancer Society, has been issued under the title, "Smoking : Lung Cancer?". Though the contents are not competible with T.I.R.C. policy, they were greatly and helpfully modified from the original manuscript. A number of outstanding cancer scientists contributed suggestions for editing this manuscript and modifying its original strong indictment of cigarettes.

16. Gathering, analyzing, preparation and distribution of various materials continued. The Research Program booklet was mailed to all doctors and scientific journals and institutions, including the membership of the American Association for Cancer Research. Reference files of relevant abstracts from pertinent scientific articles are being augmented for a wide variety of uses, including individual requests from students and scientists, newspaper and magazine writers, and industry members. Useful magazine and newspaper articles are reproduced, when permission is obtained, and made available to public information media.

OUTLOOK FOR IMMEDIATE FUTURE

At this particular moment, the immediate past looks better than the immediate future.

The next major public problem will be the second Hammond-Horn report. This is now scheduled to be given before the American Medical Association meeting from June 6 to 10 in Atlantic City.

There is no reason to hope that the second report will be in any way better than the one last year.

There is no reason to hope that it will not result in widespread attention in the press. The A.M.A. meeting this year is closer to the major news centers than it was last year in San Francisco.

The program of the Tobacco Industry Research Committee should help maintain press and public perspective on the findings reported by Drs. Hammond and Horn.

PROPOSALS FOR IMMEDIATE FUTURE

The Tobacco Industry Research Committee first appeared before the public with an assurance that the industry itself would assume leadership in research into all aspects of tobacco use and health. The industry is now moving into a position of leadership.

This brings with it a greater responsibility to the press and the public. The T.I.R.C. will have to live up to the expectations it has created on two fronts:

First, by pushing ahead soundly but steadily to get at the facts through widespread scientific investigation;

Second, to report to the public where it stands in the search for the desired information about cancer and its causes, as well as the relationship of tobacco use to other phases of health, and to describe to the public the nature and scope of T I.R.C.-sponsored research.

This calls for a more active and outspoken position. No longer can we expect the press and public to accept the terse comment that "nobody knows any answers."

Positive steps being planned and recommended for the immediate future, in brief, are as follows:

1. A strong affirmative report in mid-May by Dr. Little of where the problem stands today and what progress has been made through the efforts of the T.I.R.C. This should be a prepared statement distributed to the press and accompanied by a discussion with Dr. Little, science and other writers participating.

2. Carefully spaced distribution of basic informational material designed to implement the position set forth by T.I.R.C. This will include:

a. Through PAGEANT magazine, the article by Dr. Rienhoff is now going to important information media.

b. A reprint of Dr. Herbert Arkin's article analyzing the Hammond-Horn methods, will be ready for mailing to media the latter part of May.

c. A special report of the fight against lung cancer -- the Pfeiffer manuscript -- which will put the cigarette issue in its proper perspective. This should be set for sometime in May or June.

d. Reproductions of news reports quoting prominent medical or scientific figures who caution against condemning cigarettes on the basis of present evidence.

e. Announcement of new grants bringing the total to more than $450,000 actually approved for specific research. This is ready to go at any time but perhaps should be held for release coincidentally with Dr. Little's press conference.

3. A strong positive statement is being prepared to serve as the Tobacco Industry Research Committee's comment on the new Hammond-Horn report. This should be a statement from Mr. Hartnett, re-emphasizing the affirmative approach.

Exhibit 18

Mr. Richard W. Darrow

May 25, 1955

Carl Thompson

Messrs. Hill
Goss
Hoyt
Kahn

The following is a rundown of the status of certain steps being taken in anticipation of the June 6 presentation of the second Hammond-Horn report at Atlantic City:

1. Reprints of the Dr. Rienhoff article in Pageant were mailed on May 6 to our complete lists of public information media. Fairly good newspaper response, both editorial and news, have already been noticed.

2. Dr. Little's press conference, held May 16, resulted in fairly good publicity. Copies of this statement and press release went to our complete lists. The statement is being printed in a 3-5/8" x 8½" pamphlet for further distribution.

A request for 300 additional copies has already been received from one local medical group in Pennsylvania for distribution to its members.

3. On Monday, May 23, reprints from the Arkin article in Current Medical Digest were mailed to our complete lists. This was a followup to the original publication of the article and press release which was sent out by the Digest at that time.

4. An announcement of grants, bringing the total to date to $490,000, is being prepared for release Wednesday, June 1, with a mailing scheduled for Friday, May 27.

5. Recordings of the "Growing Old Symposium," featuring a discussion on smoking with Dr. Hess, etc., which we all have heard and transcripts of which we have, have been sent out to certain key radio stations and some report of their use, or intended use, have already been received.

6. A brief report on Dr. Little's press conference was prepared for the radio-TV news service, AIR LINES, and distributed through that organization in their service of May 20.

7. Two editorials are scheduled for distribution by the U. P. Press Association. The first is a brief summary of Dr. Little's press discussion, which will go out in the May 25 U.P.A. report. The second, scheduled for the June 2 mailing of the report, is a comment on the Dr. Arkin article.

8. Efforts have been made to provide all the assistance possible in making the two Murrow shows, scheduled for May 31 and June 7, as timely and positive as possible.

9. Arrangements have been made -- and will be covered in detail under a separate memorandum -- for transcribing pertinent sections of the Murrow show immediately after its presentation, and providing copies of these transcripts to major news outlets in New York early in the morning following the show.

10. Arrangements have been made for coverage of the A.M.A. meetings, including the symposium at the American College of Chest Physicians in Atlantic City on June 2, which will include Dr. Ochsner among the participants.

Leonard Zahn plans to go to Atlantic City, Thursday, June 2, and return Tuesday, June 7. We have been assured that he will be given press privileges to attend the various sessions (arranged through Ben Fillic in Chicago).

In addition, Jack Geiger plans to attend the meeting but exact arrangements for him have not yet been confirmed.

11. Drafts of the statement to be issued at the time of the Hammond-Horn report are in preparation -- and probably will continue to be up until the last minute.

The following are less directly related:

12. The proposed Argosy piece, by Dick Reddy, is now scheduled for the August issue and the latest revision we have seen in proof form shows that it will be an extremely positive piece.

13. A new magazine entitled Male Illustrated carries a positive piece by Albert Abarbanel. This is the first issue of that magazine and it is being distributed by the American News Company. The author is the same man who edited (?) wrote (?) the piece that appeared a couple of months ago in Popular Medicine.

14. An article debunking the lung cancer scare is scheduled for an early issue of the widely-read magazine, Confidential. The exact present status is not known.

15. A popularized version of the Pfeiffer piece has been submitted for consideration by American Weekly and no current information is available on its status.

16. The proposed Dr. Harry Greene book has been submitted to the chairman of the Law Committee for an opinion as to TIRC's distribution of this, when published, to scientific and public libraries. This book could probably hit late in the fall if everything goes well -- especially with Mr. Whiteside.

17. No definite moves have been made yet concerning the possibility of a prominent statistician (Arkin?) for meeting with the press shortly after the Hammond-Horn report. This project should be forced up.

C. P.

CT:tm

Exhibit 13

HILL AND KNOWLTON, INC.

TIRC 1956
B30 F. PR Report

ATTACHMENT #1

HK 76

CONFIDENTIAL

PUBLIC RELATIONS REPORT

to the

TOBACCO INDUSTRY RESEARCH COMMITTEE

February 14, 1956

General Introduction

The period immediately ahead will produce a considerable number of scientific papers, medical meetings and public statements both generally and specifically concerned with the subject of smoking and health. Additional reports, meetings, books and articles will focus still more attention on this subject in the next four months.

With respect to this increased activity, however, two points should be recognized:

1. A large proportion of the attacks against smoking made recently, and expected to continue in the next few months, originate with the same small group of critics who have led the anti-tobacco moves of the past two or three years.

2. Neither the press nor the public seems to be reacting with any noticeable fear or alarm to the recent attacks.

This outlook does not warrant any attitude of complacency in our public relations approach, especially when we consider what could be the impact on the public of a possible announcement (which has been rumored) by researchers alleging that they have isolated and identified a carcinogen in tobacco. Also, it is not possible at this time to assess fully the probable impact of federal government reports and activities that are indicated in the months ahead.

With a number of grantees at or near the stage of public reporting on their research to date, the conduct of the Tobacco Industry Research Committee will be closely scrutinized by the scientific world, as well as the press, as to the stand and attitude assumed toward those reports. Protection of the integrity of the industry's position in this regard is vitally necessary, and conclusive reaffirmation that true freedom of thought and action has been given TIRC grantees can be rewarding.

Our public relations efforts will continue to be directed toward: (a) keeping the press well informed of the balancing aspects of the situation as new attacks arise, and (b) increasing the prestige of TIRC's own efforts by showing that TIRC is helping to gain the needed facts through adequately financed and carefully planned scientific research.

The research program of the Scientific Advisory Board has now progressed to a point warranting fuller description of its accomplishments and aims within the fields of science and medicine. With the valuable guidance and assistance

of Drs. Little and Hockett, steps are being worked out to give doctors and scientists greater knowledge of the scope, composition and nature of the program.

Meanwhile, the TIRC continues increasingly to benefit from the leadership which Dr. Little, Dr. Hockett and the members of the SAB are providing. Dr. Little's forthcoming editorial and speeches will be a further contribution to the prestige of the TIRC research program.

The Recent Months

A factor that has become more noticeable since the last TIRC meeting is that, more and more, doctors and scientists are voluntarily speaking up at medical meetings to express disagreement with the flat charges made against tobacco. They do not exonerate tobacco but say that the case against smoking has not been proved and that much more evidence is needed.

Another aspect that also is becoming more apparent is the greater emphasis being placed by scientists in this country and abroad on the role of air pollution as the major cause of lung cancer. Two recent scientific reports on air pollution and health received national newspaper attention. The subject is being treated by the press as a new, interesting and important phase of the overall situation.

Meanwhile, reports adverse to tobacco from two major sources, which previously received much publicity, were largely ignored by the press in recent months because of their apparent failure to contribute anything pertinent or different to the problem.

In England the situation as regards the press appears to be quite different than that in this country. There is frequent and increasing mention of attacks on smoking in the British press.

The Future

Smoking and health will be the subject of many papers and symposia at scientific meetings during the next several months. Some of the papers will be given by TIRC grantees, one of whom is scheduled to present an exhibit and paper at three medical meetings. Several grantees have submitted papers on their research findings to date for publication in professional journals.

Reports by grantees, whether they are made at meetings or appear in scientific journals, may lead to requests from the press for comment by TIRC. Regardless of what the reports say, TIRC intends only to restate its guarantee of complete scientific freedom to those who have received, and will receive, research grants. Such action will enhance the acceptability and sincerity of TIRC's research program with the scientific world and the public at large.

Several TIRC grantees already have presented papers at separate medical meetings but none received any press mention.

Meetings at which smoking and health are expected to be discussed:

1. Feb. 24, Long Island sub-section of the American Chemical Society, Brooklyn. The entire day is devoted to tobacco. The morning session, to be

(Page 3 is missing)

3. The NCI is doing a retrospective study of lung cancer and smoking habits in women.

4. Dr. Wynder, in collaboration with a statistician at the National Institutes of Health, is reported preparing a paper from Wynder's material relating to lung cancer statistics in women. (This may be one of the papers Dr. Wynder will present in April.)

5. The Veterans Administration study is continuing.

6. Two government health statisticians are studying old VA records with regard to influenza, gas exposure and other respiratory conditions of men in World War I. This study will be compared with the VA study.

7. The NCI is considering a retrospective study that also would make use of the Census Bureau survey. This would replace the previously proposed study of the relationship of smoking to mortality among women employed by the government and covered by federal employe insurance. The latter plan has been dropped, at least for the present.

Other factors of public relations interest to TIRC are Dr. Little's forthcoming report (in May) on the progress and accomplishments of the research program, the talks he will give at three medical meetings and the editorial he has written for CANCER RESEARCH, official publication of the American Association for Cancer Research.

Dr. Little will speak March 5 before the Wayne County Medical Society in Detroit. On June 5 he will present a paper at a symposium on "Cancer of the Lung" at the Third National Cancer Conference in Detroit. On June 7 he will speak at a symposium on "The Present Concept of Bronchogenic Carcinoma" at the annual meeting of the American College of Chest Physicians in Chicago.

The Third National Cancer Conference is co-sponsored by the American Cancer Society and the National Cancer Institute. The planning committee for the meeting has suggested to Dr. Little that he speak on "Etiology and Lung Cancer -- Tobacco" and also has asked him to participate in a panel discussion on etiology.

The editorial Dr. Little has written and the talks he is to give will increase scientific appreciation of the research program and will be of interest to science reporters in their normal coverage of such occurrences.

Cancer Month

April has been designated "Cancer Month" and during the next few months the American Cancer Society will conduct an active campaign to achieve its goal of $26,000,000. The build-up has been apparent in recent weeks:

1. An article on lung cancer and smoking by Dr. Charles Cameron, the ACS' medical and scientific director, appeared in the January issue of THE ATLANTIC. Virtually the entire text was word for word from his report of 1953-1954. The ACS wrote a news release on the article which was released to local newspapers by various ACS divisions.

Dr. Cameron also has written a book, "The Truth About Cancer," which is expected to be published in March. The book contains a section on smoking and lung cancer and will be promoted nationally by the ACS.

2. The Feb. 10 issue of U.S. NEWS & WORLD REPORT featured an interview with Dr. C. P. Rhoads, director of the Sloan-Kettering Institute, on "Is A Cancer Cure Near?" One section dealt with Dr. Rhoads' conclusions on cigarette smoking as a cause of lung cancer.

3. The lead article in the Feb. 8 issue of the WALL STREET JOURNAL was on cancer chemotherapy. The February issue of McCALL'S magazine has a human interest article based on Sloan-Kettering. The science editor of Scripps-Howard Newspaper Alliance carried a column on cancer Feb. 7.

4. Columnist Ed Sullivan is national campaign chairman for the ACS drive. In his syndicated column of Feb. 5, Sullivan said that cancer research doctors "are planning a statement that will jolt the country in March."

This may be a report by Dr. Wynder and his associates alleging that they have isolated a carcinogen in tobacco. On Dec. 27, 1955, speaking from the floor at a "Lung Cancer-Tobacco Controversy" session at the American Statistical Association meeting, Dr. Wynder said that he will announce soon the isolation of a substance in cigarette smoke, "not benzpyrene but a member of the benzpyrene family," which has, in every instance, produced tumors in animals.

5. The March issue of READER'S DIGEST has a condensation of an anti-smoking editorial that appeared in the December 1955 issue of SOUTHWESTERN MEDICINE, journal of three southwestern medical societies.

6. The June issue of GERIATRICS will be devoted entirely to the subject of cancer and will have an editorial written by Dr. Cameron.

Highlights of Recent Activities

1. The biennial report of the Sloan-Kettering Institute, issued Dec. 7, purported to disclose "new" evidence linking smoking to larynx cancer. The report also dismissed air pollution as a possible causative factor in lung cancer. A TIRC statement was released to help put the report in factual perspective. General press treatment of the report did not stress the smoking and health sections.

2. Two papers on benzpyrene in cigarette paper and tobacco were given by the Rand Development Corporation before the American Association for the Advancement of Science meeting at Atlanta, Ga., Dec. 27. Hill and Knowlton, Inc., arranged for coverage of the meeting at which the Rand company's claims were challenged by Dr. Louis Fieser, a Harvard University professor who is an authority on benzpyrene and related compounds. The Rand papers were widely publicized and Dr. Fieser's comments also appeared in many of the newspaper stories.

3. Dr. Hammond and Dr. Berkson appeared on the same platform Dec. 27 at a session on the "Lung Cancer-Tobacco Controversy" at the meeting of the American Statistical Association in New York. The American Cancer Society made available a release on Dr. Hammond's paper but none was issued on Dr. Berkson's talk either by his own organization or the statistical group. There was little press mention of this session.

4. A report from a New Zealand public health official, published in a British medical journal, attributed the increase in lung cancer incidence to air pollution and not to smoking. Advance information of the date of publication was obtained from contacts in New Zealand and England and when it appeared it was brought to the attention of the United States press. Stories and editorials on it appeared in many newspapers.

5. A paper by Dr. Hueper appeared in a publication of the U. S. Public Health Service in January. Advance copies of the article, which described cigarettes as only a minor possible contributory factor, if any, in lung cancer, were obtained and distributed. Stories were carried by several news wire services and appeared in newspepers throughout the country. It also was mentioned on many radio and television news broadcasts.

6. A book on the scientific aspects of smoking and health, being written by science writer Eric Northrup, is expected to be published by June 1.

7. A year-end statement by Mr. Hartnett was released to and published in a number of the tobacco trade magazines.

8. Releases were issued on new TIRC grants and the addition of $500,000 to the research fund, and stories on both appeared in many newspapers. A story has been prepared for release at an appropriate time on the continuance and expansion of the TIRC medical student fellowship program.

9. The editor of a company which prepares pamphlets for employe reading racks requested information for a proposed pamphlet on smoking and health. He later decided to discard the smoking and health angle and instead is planning a condensation of a 1954 popular-priced book on "How To Stop Smoking."

10. The 1956 WORLD ALMANAC was published and contains a balanced treatment of the subject of smoking and health. Informational material was given the editor several months ago.

11. Informational material, both from TIRC and other sources, continued to be supplied to large numbers of doctors, scientists, science writers, students and others interested in smoking and health

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Exhibit 14

HILL AND KNOWLTON, INC.

CONFIDENTIAL

HK 20

July 19, 1956

CONFERENCES WITH LIFE AND
READER'S DIGEST, JULY 17-18, 1956

MEMORANDUM TO: Mr. Timothy V. Hartnett

This memorandum will summarize our contacts with LIFE staff members on July 17, and DeWitt Wallace, editor of THE READER'S DIGEST, on July 18. Participants on behalf of TIRC were Dr. Little and Messrs. Hartnett and Darrow.

LIFE Contact

This was a luncheon-meeting initiated at the invitation of Mr. Robert T. Elson, Deputy Managing Editor of LIFE.

Those attending for LIFE were: Mr. Elson; Albert L. Furth, assistant to the editor-in-chief; George Hunt, assistant managing editor; Warren Young, science editor; Ed Kern, science writer; Hugh Sidey and Miss Alix Witteborg, science researchers.

In extending the original invitation, Mr. Elson stated an interest in having LIFE'S science staff gain a fuller appreciation of Dr. Little's personal views on the subject of cancer generally, particularly his estimate of the importance of factors within the individual as opposed to external stimuli.

At the luncheon, which was conducted in a friendly and congenial atmosphere, Mr. Elson asked Mr. Hartnett to open the discussion by outlining the thinking behind the formation of TIRC and describing its organizational set-up. A number of interested questions were prompted by Mr. Hartnett's description of TIRC policies. Particular note was taken of the freedom of action given the SAB, as well as grantees.

Dr. Little then covered a number of aspects of the broad subject of cancer in a brief talk along much the same lines as his presentation at the last meeting of the TIRC on February 14, 1956.

He pointed out the importance to the public of receiving a balanced presentation of all the facts and underscored the need for editorial responsibility in handling stories that rouse unwarranted fears.

Questions from those present indicated an active interest in what Dr. Little had to say. While their schedules did not permit as much discussion as might have been desired by several of the LIFE staff members, it was pointed out that Dr. Little would be happy to talk further on those items of special interest to them at a later date of their choosing.

Arrangements were made to send along certain materials of interest to the LIFE staff members. A visit to TIRC and Hill and Knowlton, Inc., by some of the editors and writers is to be arranged at an early date. This will provide an opportunity for up-dating on the scope and nature of information available and provide further knowledge of how TIRC and SAB operate. An opportunity of the LIFE staffers to meet Dr. Hockett will be provided on the occasion of that visit.

READER'S DIGEST Contact

This was an afternoon meeting at the READER'S DIGEST headquarters offices near Pleasantville with DeWitt Wallace, editor, and James Monahan, senior editor and Lois Mattox Miller, roving editor, attending for the publication and Dr. Little, Mr. Hartnett and Mr. Darrow for TIRC.

This was a most pleasant and congenial discussion.

Mr. Wallace said that through Mr. Monahan and Mrs. Miller he had a good understanding of TIRC and what it was doing but would welcome knowing more about it.

Mr. Hartnett briefly outlined the background of TIRC, discussed some of the problems in organizing an industry approach to the question and made clear the open-minded approach that had been adopted.

Dr. Little stressed importance of the public not being stampeded into undue fears and the great responsibility held by major publications to keep the public adequately informed so that they would not tend to over-simplify the problem and expect a "push-button answer" to problems so complex as cancer and heart disease.

Mr. Monahan expressed the belief that the Scientific Advisory Board and Dr. Little had thoroughly dissipated any skepticism about the sincerity of the TIRC program and the industry's support of it. He commented that a phenomenally good job had been done in getting the research program under way so quickly on such a sound basis.

Both he and Mrs. Miller indicated considerable knowledge of TIRC but said they wanted to be even more closely kept up to date in the future. They also asked to be alerted on all materials of significance dealing with any aspect of tobacco and health. Copies of the June, 1956, issue of CANCER RESEARCH, including an article by Dr. Kotin; CANCER NEWS, including the American Cancer Society story on environmental cancer, and a recent Armour Research bulletin, including a report on air pollution research, were given to Mr. Monahan as samples of the recent literature of interest.

The recent Robert Buck article "Why an Airline Pilot Quit Smoking" was discussed with Mr. Wallace. He expressed surprise that their Research Department had not caught the error which referred to 900 people involved in tests as "airmen" when they were actually college students.

Both Mr. Monahan and Mrs. Miller expressed interest in visiting TIRC and Hill and Knowlton, Inc., offices to gain a better knowledge of data and services available which might be helpful to them on future assignments. Mr. Wallace said they would be happy to talk further any time we felt it was warranted.

Hill and Knowlton, Inc.

Cautery
WATCH —
MONAHAN

Exhibit 15

R J Reynolds Tobacco Company
[illegible]

RJR

January 11, 1990

Principal
Willow Ridge School
480 Willow Ridge Drive
Amherst, NY 14150

Dear Sir or Madam:

A number of your fifth grade students have written R.J. Reynolds Tobacco Company commenting that they do not feel our company should allow the use of our brand names on children's toys and candy cigarettes.

As information, R.J. Reynolds Tobacco Company's policy is not to allow our brand names to be used on toys or candy cigarettes and any current use of our brand names in this fashion is not sanctioned by our company.

Some of the students also commented about the controversies surrounding cigarette smoking. The tobacco industry considers smoking to be a custom for those adults who derive pleasure from it. We believe that whether to smoke or not is a decision that should be freely made by individuals who have reached the age of mature judgment. Accordingly, our advertising is directed to adult smokers and not younger people.

The tobacco industry is also concerned about the charges being made that smoking is responsible for so many serious diseases. Long before the present criticism began, the tobacco industry, in a sincere attempt to determine what harmful effects, if any, smoking might have on human health, established The Council for Tobacco Research--USA. The industry has also supported research grants directed by the American Medical Association. Over the years the tobacco industry has given in excess of $162 million to independent research on the controversies surrounding smoking -- more than all the voluntary health associations combined.

Despite all the research going on, the simple and unfortunate fact is that scientists do not know the cause or causes of the chronic diseases reported to be associated with smoking. The

R.J. Reynolds Tobacco USA
Winston-Salem NC 27102

Principal
Page Two
January 11, 1990

answers to the many unanswered controversies surrounding smoking -- and the fundamental causes of the diseases often statistically associated with smoking -- we believe can only be determined through much more scientific research. Our company intends, therefore, to continue to support such research in a continuing search for answers.

We would appreciate your passing this information along to your students. You may also be interested in the enclosed publications presenting the position of our company and the tobacco industry on the issue of youth smoking.

Sincerely,

Jo F. Spach

(Mrs.) Jo F. Spach
Manager, Public Information
Public Relations Department

JFS/jmd

Enclosures

Exhibit 16

CTR Special Projects

Researcher	Project Title/ Description	Period	Budget	Date Approved
Thomas F. Mancuso	"Demographic Studies of Mortality in Ohio" (Step-by-step progression of identification of high risk population sub groups and attempts to determine specific causes for high risk)	36 months (In letter dated 3-3-79, stated he planned to write report "this summer")	$38,100	October 1975; July of 1978 requested 13-month extension without additional funds for completion of work
Eleanor MacDonald	"Regional Patterns of Cancer of Major Sites in 5 Large Regions of Texas & Regional Patterns of Mortality in Houston, 1940-1960" (Study of factors associated with high cancer mortality rates in states or regions of U.S.)	4 years; project funded through January 1979 (one-year extension under consideration)	$98,171 ($106,441)	Latest extension approved August, 1977 (Approval pending)
Kenneth Moser	Investigation of Potential Role of Polymorphonuclear Leucocyte Elastase Concentration in Pathogenesis of Emphysema	3 years	Total projected cost from $196,000 to $312,000	December, 1976
Ingram Olkin	"A Study of the Models Used in the Analysis of Certain Medical Data" (Review of the appropriateness of treating biomedical data with the multivariate techniques of assumed normality)	2 years (Final report being prepared)	$12,000	Letter of Confirmation from CTR dated 6-19-78

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CONFIDENTIAL

April 1, 1981
[Personal & Confidential—
For Counsel Only]

CTR Special Projects

Researcher	Project Title/ Description	Period	Budget	Date Approved
John B. Carter	Autopsy study designed to examine accuracy of lung cancer diagnoses (investigators checking autopsy records of University Hospitals for period extending from 1948 to 1978 for errors in diagnoses)	See publication in Cancer July 1, 1980	$86,305; addition of $5,700 approved 8-29-77 to locate and analyze past medical histories of patients who died early in project	June, 1978
H. J. Eysenck	Maintenance of Twin Registry	2 years (through 6-80)	$30,000 total; $6,600 for cost overruns	March, 1979 July, 1977
Alvan R. Feinstein	Support biostatistician, Carolyn K. Wells, to assist Dr. Feinstein	Completed 1980	$50,000	June, 1976
Arthur Furst	Study the Effects of Combined Asbestos and Benzo(a)pyrene on lungs of mice	2 years; data currently being analyzed	$61,500	March, 1977
			$3,000 additional for increased cost of slides	December, 1978
Richard Hickey	"Epidemiological and Etiological Studies on the Relation of Air Pollution, Smoking and Other Environmental Variables to Human Chronic Diseases"	1-1-81 to 12-31-81	$83,912	March, 1981

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PLAINTIFF'S EXHIBIT
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CTC Special Projects

Researcher	Project Title/ Description	Period	Budget	Date Approved
Duncan Hutcheon	"A pilot Project to Investigate the Environmental Pharmacology of Industrial Inhalants"	1 year	$80,010	April, 1979
		6 month extension	$15,000	July, 1980
Joe Jacks	Statistical model of lung cancer mortality	Extension through 12-31-80	$5,000	May, 1980
		Extension through 3-31-81	$15,500	Pending
Marlene La Vie	Support for graduate student to assist in basic research in field of immunopathology	Completed September, 1980	$10,000	Letters of approval dated April, 1980; letter of confirmation from CTC dated 9-11-80
Eleanor Macdonald	"Regional Patterns of Cancer of Major Sites in Three Regions of Texas: A Regional Pattern of Mortality in Houston, 1968-1969; Study of factors associated with high cancer rates in states or regions of U.S."	1 years	$100,661	Extension approved February, 1979
		5-1-80 through 4-30-81	$133,121	Extension approved May, 1980
	Funds to cover costs of retirement program as required by new Texas law		$2,010	October, 1979

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CTR Special Projects

Researcher	Project Title/ Description	Period	Budget	Date Approved
Thomas F. Hancuse	"Demographic Studies of Mortality in Ohio" Step-by-step progression of identification of high risk population sub-groups and attempts to determine specific causes for high risk)	12 months (said he plans to write report summer of 1980.)	$10,100	October, 1979; July of 1978 requested 12-month extension with additional funds for completion of work
	Low level radiation study		$10,000	March, 1979
Kenneth Moser	Investigation of Potential Role of Polymorphonuclear Leucocyte Elastase Concentration in Pathogenesis of Emphysema	Completed; No report yet	Total projected cost for study $110,000 to $111,000	December, 1978
Ingram Olkin	"A Study of the Models Used in the Analysis of Certain Medical Data" (Review of the appropriateness of treating biomedical data with the multivariate techniques of assumed normality)	Completed	$12,000	Letter of confirmation from CTR dated 4-19-78
Charles Peplis/ Jay Adams	"Adaptation to Components of Tobacco Smoke: Role of Components of the Lung to Oxidants contained in Cigarette smoke; Adaptation of the Heart to Alcoholic Effects"	1 year	$44,000	December, 1980
Gorman Riley	Three year program of studies on stress physiology	1st year	$159,000	April, 1981

CONFIDENTIAL

C.19.CTR

CTR Special Projects

Researcher	Project Title/ Description	Period	Budget	Date Approved
Henry Rothschild	Second extension of pilot study examining disproportionately high mortality rates of respiratory tract cancer in southern Louisiana to determine if genetic and environmental factors are possible causes (Rigdon helping). Extension includes an investigation of respiratory cancer and employment in sugar cane industry	1 year, 1980-81	$61,[illegible]	July, 1980
	Third extension concentrating on identification of families in which lung cancer has developed.	1 year, 1981-82	$16,000	pending
Henry Russek/ Linda Russek	"Behavior Patterns and Strategies for the Mastery of Stress, Anxiety Reduction and Perceptual Functioning" is comparison of the efficacy of different methods of relaxation in the face of stress; a study of differences between Type A and Type B individuals	12-18 months	$18,500	December, 1979
John Salvaggio	Investigation of Physical, Chemical and Immuno-Chemical Properties of Components Present in Tobacco Smoke	5 years	First year received $59,850; 6-1-78 requested increase in second year budget from $[illegible] to $63,101 and in third year from $37,039 to $52,125;	May, 1978 Increase in funding approved May, 1978
			fourth year budget to $61,146	5th year approved May, 1979
			fifth year budget to $65,155	May, 1979

CONFIDENTIAL

[illegible]

CTR Special Projects

Researcher	Project Title/ Description	Period	Budget	Date Approved
Carl Seltzer	Continuation of work on constitutional differences between smokers and nonsmokers	7-1-00 through 6-30-01	$70,000	April, 1980
		7-1-01 through 6-30-02	$70,000	April, 1981
Carl Seltzer/ Don Van Den Berg	Study of Smoker/Nonsmoker differences	1 year	$56,000	September, 1980
Louis Seloff	"Immunoassay of Lecithin Cholesterol Acyltransferase after Eating and Smoking on Health and Atherosclerosis"	1 year 7-1-00 to 6-30-01	$48,910	July, 1980
Theodor Sterling	"A Continuing Critical Review of the Major Factors in the Etiology of Diseases Emerging from Statistical Studies"	7-1-77 through 6-30-80	$810,000	Letters of approval dated March-April, 1977
		Extension to 5-30-81	$101,119	March, 1980
[redacted]	"Computer Analysis of Health-Related Data" (Modification of funding procedure in main project designed to conform with governmental requirement that university facility cannot be used for nonuniversity projects)		No change in cost of project (All of project budget allocated to Simon Fraser University, remainder to original grantee)	Procedural change approved September, 1977, to begin 10-1-77

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CTA Special Projects

Researcher	Project Title/ Description	Period	Budget	Date Approved
Theodor Sterling	"Evaluation of the Interaction Between Geographic, Geocollateral, Smoking and Health Variables and Indices"	18 months	$91,710	September, 1979
	"Possibility Study on Office Environments"		$9,900 11,150 additional	July, 1980 December, 1980
Theodor Sterling/ Herald Perry	"Retrospective Analysis of Environmental Contacts of Patients with Respiratory Cancer, Other Cancers, and Other Diseases"	9-1-81 to 11-30-81 and 12-1-81 to 11-30-82	$90,022 $70,530	February, 1981 February, 1981

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PLAINTIFF'S EXHIBIT 0532

00796460

June 30, 1980
(Personal & Confidential-
For Counsel Only)

CTR Special Projects

Researcher	Project Title/ Description	Period	Budget	Date Approved
John W. Carter	Autopsy study designed to examine accuracy of lung cancer diagnoses (Investigators checking autopsy records of University Hospitals for period extending from 1910 to 1976 for errors in diagnoses)	Final report accepted for publication by Cancer (not yet published)	$96,305; additional $5,700 approved 8-30-77 to locate and analyze past medical histories of patients who died early in project	June, 1974
R. J. Hrubec	Maintenance of Twin Registry	3 years (Through 6-80)	$10,000 total; $4,600 for cost overruns	March, 1978; July, 1977
Alvan R. Feinstein	Support biostatistician to assist Dr. Feinstein	3 years	$50,000	June, 1976 (in abeyance until selection made)
Franklin Institute	Determination and characterization of tobacco glycoprotein as an artifact	3 months	$20,130	May, 1979
	Generation of 35 milligrams of artifact		$7,700	September, 1979
		Research satisfactorily completed 1-80	$3,100 for cost overruns	January, 1980

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PLAINTIFF'S EXHIBIT 0535

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CTR Special Projects

Researcher	Project Title/ Description	Period	Budget	Date Approved
Arthur Furst	Study the Effects of Combined Asbestos and Benzolpyrene on lungs of mice	2 years; data currently being analyzed	$51,500	March, 1977
			$1,000 additional for increased cost of mice	December, 1979
Richard Richey	"Epidemiological and Etiological Studies on the Relation of Air Pollution, Smoking and Other Environmental Variables to Human Chronic Diseases"	1-1-80 to 12-31-80	$90,010	Letter of confirmation from CTR for extension of project dated 1-30-80
Duncan Hutcheon	"A Pilot Project to Investigate the Environmental Pharmacology of Industrial Inhalants"	1 year	$89,070	April, 1979
		4 month extension	$15,000	Pending
Joe Jenie	Statistical model of lung cancer mortality	Through summer, 1979	$8,000	February, 1979
		Extension through 10-31-80	$6,000	May, 1980
Suzanne Snoebel	Determine reliability of non-invasive technique to measure changes in cardiac function, if any, during inhalation of tobacco smoke	1 year; preliminary report dated 1-79	$20,025	December, 1977

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CTR Special Projects

Researcher	Project Title/ Description	Period	Budget	Date Approved
Mariano La Via	Support for graduate student to assist in basic research in field of immunopathology	2 years; Assistant selected July, 1978	$24,000	Letters of approval dated April, 1978; letter of confirmation from CTR dated 9-11-78
Thomas F. Mancuso	"Demographic Studies of Mortality in Ohio" (step-by-step progression of identification of high risk population sub-groups and attempts to determine specific causes for high risk)	14 months (said he plans to write report this summer.)	$10,700	October, 1975; July of 1978 requested 13-month extension without additional funds for completion of work
	Low level radiation study		$10,000	March, 1979
Eleanor Macdonald	"Regional Patterns of Cancer of Major Sites in 5 Large Regions of Texas & Regional Patterns of Mortality in Houston, 1940-1969; (Study of factors associated with high cancer rates in states or regions of U.S.)	1 year;	$106,143	Extension approved February, 1979
		5-1-80 through 4-30-81	$133,131	Extension approved May, 1980
	Funds to cover costs of retirement program as required by new Texas law		$2,916	October, 1979
Kenneth Moser	Investigation of Potential Role of Polymorphonuclear Leucocyte Elastase Concentration in Pathogenesis of Emphysema	3 years	Total projected cost from $190,000 to $313,000	December, 1976

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CTR Special Projects

Researcher	Project Title/ Description	Period	Budget	Date Approved
Ingram Olkin	"A Study of the Models Used in the Analysis of Certain Medical Data" (Review of the appropriateness of treating biomedical data with the multivariate techniques of assumed normality)	3 years Final report sent to CTR on 7/6/79, and report for publication in progress	$13,000	Letter of confirmation from CTR dated 6-12-78
Charles Puglia/ Jay Roberts	"Adaptation to Components of Tobacco Smoke" (a study of the response of the lung to oxidants contained in cigarette smoke; adaptation of the heart to nicotinic effects)	3 years; 6 month extension obtained from CTR with an increase in funding	$44,814	May, 1977
Henry Rothschild	Second extension of pilot study examining disproportionately high mortality rates of respiratory tract cancer in southern Louisiana to determine if genetic and environmental factors are possible causes (Sigdon helping) Extension includes an investigation of respiratory cancer and employment in sugar cane industry	1 year	$15,331	June, 1979
Henry Russek/ Linda Russek	"Behavior Patterns and Strategies for the Mastery of Stress, Anxiety Reduction and Perceptual Functioning" (a comparison of the efficacy of different methods of relaxation in the face of stress; a study of differences between Type A and Type B individuals)	12-18 months	$48,300	December, 1979

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CTR Special Projects

Researcher	Project Title/ Description	Period	Budget	Date Approved
John Salvaggio	Investigation of Physical, Chemical and Immuno-Chemical Properties of Components Present in Tobacco Smoke	6 years	First year received $39,090; 6-1-76 requested increase in second year budget from $40,705 to $47,101 and in third year from $37,070 to $57,775;	May, 1976 Increase in funding approved May, 1977
			Fourth year budget is $67,146	4th year approved May, 1979
			Fifth year budget is $65,755	May, 1980
Carl Seltzer	Continuation of work on constitutional differences between smokers and nonsmokers	7-1-79 through 6-30-80	$70,000	April, 1979
		7-1-80 through 6-30-81	$70,000	April, 1980
Theodor Sterling	"A Continuing Critical Review of the Major Factors in the Etiology of Diseases Emerging from Statistical Studies"	7-1-77 through 6-30-80	$610,000	Letters of approval dated March-April, 1977
		Extension to 9-30-81	$703,110	March, 1980

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CTA Special Projects

Researcher	Project Title/ Description	Period	Budget	Date Approved
Theodor Sterling	"Computer Analysis of Health-Related Data" (Modification of funding procedure to main project designed to conform with governmental requirement that university facility cannot be used for nonuniversity projects)		No change in cost of project ($50 of project budget allocated to Simon Fraser University; remainder to originial grantee)	Procedural change approved September, 1971, to begin 10-1-71
	"Evaluation of the Interaction Between Geographic, Generational, Banking and Health Variables and Indices"	18 months	$14,710	September, 1970
Theodor Sterling/ Harold Perry	"Retrospective Analysis of Environmental Contacts of Patients with Respiratory Cancer, Other Cancers, and Other Diseases"	3 years	$133,933 $17,436 additional	Letters of approval dated October, 1970 November, 1970

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February 2, 1979
(Personal & Confidential
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CTR Special Projects

Researcher	Project Title/ Description	Period	Budget	Date Approved
Domingo Aviado	"Cardiopulmonary and Renal Vascular Effects of Constituents of Tobacco Smoke"	7-1-77 through 6-30-78 (extended without increase in budget to December, 1978)	$85,000	May 1977; proposal to transfer project from Pennsylvania to New Jersey approved 1-8-78
Victor Buhler	Spend about 40 hours a month reviewing current literature of interest	January through December, 1977 (extended without increase in budget to December, 1978)	$10,000	January, 1977
John B. Carter	Autopsy study designed to examine accuracy of lung cancer diagnoses (investigators checking autopsy records of University Hospitals for period extending from 1910 to 1974 for errors in diagnoses)	7-1/2 years (final report being revised for submission to medical journal)	$86,309; additional $5,700 approved 8-29-77 to locate and analyze past medical histories of patients who died early in project	June, 1971

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CTR Special Projects

Researcher	Project Title/ Description	Period	Budget	Date Approved
W. J. Dyscnch	Maintenance of Twin Registry	3 years	$15,000 or $30,000	March, 1978
Alvan R. Feinstein	Support biostatistician to assist Dr. Feinstein	3 years	$30,000	June, 1978 (in abeyance until selection made)
T. M. Finley	Construct "lung" model consisting of lipid layer, enzyme, and protein to test activities of lipid monolayer, especially effects on enzyme activity	6 months to 1 year (Draft report being prepared)	$30,000	Letters of approval dated February, 1977
Roswell Institute	Isolate 5 gm. of tobacco glycoprotein from tobacco smoke condensate and tobacco leaf	6 months (Draft of final report has been prepared)	$31,050	Letter of confirmation from CTR dated 6-1-78
Arthur Furst	Study the Effects of Combined Asbestos and Benzo(a)pyrene on lungs of mice	3 years	$61,100	March, 1977

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CTR Special Projects

Researcher	Project Title/ Description	Period	Budget	Date Approved
Richard Richey	"Epidemiological and Etiological Studies on the Detection of Air Pollution, Smoking and other Environmental Factors Relation to Human Chronic Diseases"	1-1-79 to 1-31-79	$10,161	Letter of confirmation from CTR for extension of project dated 3-3-79
Susanne Snoebel	Determine reliability of non-invasive technique to measure changes in cardiac function, if any, during inhalation of tobacco smoke	1 year	$11,025	December, 1977
Marlene La Vie	Support for graduate student to assist in basic research in field of immunopathology	2 years; Assistant selected July, 1978	$14,000	Letters of approval dated April, 1978; letter of confirmation from CTR dated 9-15-78

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CTR Special Projects

Researcher	Project Title/ Description	Period	Budget	Date Approved
Henry Rothschild	Extension of pilot study examining disproportionately high mortality rates of respiratory tract cancer in southern Louisiana to determine if genetic and environmental factors are possible causes (Pigdon helping)	1 year	$[illegible]	April, 1978
John Salvaggio	Investigation of Physical, Chemical and Immuno-Chemical Properties of Components Present in Tobacco Smoke	3 years	First year received $[illegible]; 5-1-76 requested increase in second year budget from $[illegible] to $[illegible] and in third year $[illegible] to $[illegible]	May, 1976; Increase in funding approved May, 1977

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CTR Special Projects

Researcher	Project Title/ Description	Period	Budget	Date Approved
Carl Baltrop	Continuation of work on constitutional differences between smokers and nonsmokers	7-1-70 through 6-30-75	$60,000	May, 1970
Theodor Sterling	"A Continuing Critical Review of the Major Factors in the Etiology of Disease Foreign from Statistical Studies"	7-1-77 through 6-30-80	$810,000	Letters of approval dated March-April, 1977
	"Computer Analysis of Health-Related Data: Modification of funding procedure in main project designed to confirm with general medical requirement that university facility cannot be used for non-university projects)		No change in cost of project $110 of project budget allocated to Simon Fraser University, re-ceived as original granted	Procedural change approved September, 1977, to begin 10-1-77
Theodor Sterling/ Harold Perry	"Retrospective Analysis of Environmental Contents of Patients with Respiratory Cancer, Other Cancers, and Other Diseases"	3 years	$117,932	Letters of approval dated October, 1978

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want to computerize the results for a more precise appraisal. We now have such intensive data for about 1200 patients with these three cancers, and the use of a computer is desirable for the analyses.

The main need in this type of work is trained human personnel to assist in the painstaking, arduous task of reviewing records, confirming facts, and coding data. From funds made available to me by the West Haven VA Hospital, I shall have support for two people who have currently been working on this project. The work really requires at least two more people, however, and the funds I am looking for will be to support these other two people.

I currently have placed grant applications with two different agencies that will announce their decisions in mid-December. Should both agencies reject the applications——a strong possibility in this era when no one seems to want to support clinical research——I shall need the help I have cited until I can compose additional new grant applications to other agencies for support after June 30, 1966.

If you want reprints, further descriptions, or any other information about this matter, please let me know. I shall be most grateful for any help you and your colleagues can provide.

Sincerely yours,

Alvan R. Feinstein, M. D.
Associate Professor of Medicine

ARF/lp

CONFIDENTIAL

University of Hawaii at Manoa

Behavioral Biology Laboratory
Pacific Biomedical Research Center
Snyder Hall 113 • 1348 The Mall • Honolulu, Hawaii 96822
Telephone: 948-6955

April 11, 1975

Mr. Edwin J. Jacob
Jacob & Medinger
1270 Avenue of the Americas
Rockefeller Plaza
New York, N.Y. 10020

Dear Ed:

This letter is for the purpose of recording the essential features of our recent telephone conversations concerning the funding and operation of the pending research program on genetics and tobacco-related behaviors.

It has been agreed by the investigators that I should serve as coordinating investigator. In this role, I would serve as the communication link between the investigators and the granting consortium. I would be responsible for coordinating the preparation and submittal of required fiscal and scientific progress reports and arranging for periodic meetings of the consulting and review panel.

Responsibility for the scientific conduct of the research would be assumed by the principal investigators of the three separate projects, as follows:

Hawaii study -- Geoffrey Ashton

Half sib-twin study -- Wilson Crumpacker and
Steven Vandenberg

Animal study -- Gerald E. McClearn

PLAINTIFF'S EXHIBIT 0529

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The principal investigators would be responsible for expenditures on their particular projects, and would have freedom to transfer funds among budget categories as required. With mutual consent of the principal investigators involved, funds could be transferred between projects. However, all expenditures would be made in compliance with the applicable state and University rules of Colorado or Hawaii, as relevant.

The consulting and review panel will be composed of scientists mutually acceptable to the investigators and to Dr. William Gardner. After a period of approximately 18 months, a meeting of the consulting and review panel will be convened to evaluate progress of the projects and to make recommendations to the grantors concerning continuation of support. In the case of a recommendation to discontinue a project, funds for phasing out the operations will be continued at least in amount sufficient to meet staff personnel obligations for a period up to an additional six months, depending on the terms of employment.

Assuming that obligations have been undertaken to employ staff through the full second year, the amount of savings from the second year budget that would be made by termination of data collection and analysis after 18 months would be approximately as follows:

Hawaii study -- $82,076

Half sib-twin study -- $50,737

Animal study — $27,268

If obligations are undertaken only to provide 60-day notice of termination of employment, then additional savings in the amounts of $7,400, $5,000 and $40,000, respectively might be made.

If the circumstances are such as to warrant a continuation of data collection and analysis during the phase out period, a negotiated amount not to exceed the budgeted amount for the next six months, but with a longer time limit for expenditure, will be made available.

In the event of favorable recommendation at the time of evaluation, research support will be continued, and a second evaluation meeting will be held approximately at the end of 27 months. The purpose of this meeting will be to evaluate progress and to make recommendations regarding funding for the fourth and fifth years of the study.

I am anxious to know if the above is an accurate summary of the principal points of our discussions.

Sincerely,

Gerald E. McClearn

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

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SAN FRANCISCO, CALIFORNIA 94122

SCHOOL OF MEDICINE
DEPARTMENT OF MEDICINE

Direct: (415) 666-1711

Section of Hematology and Immunology

July 20, 1972

Mr. Edwin Jacob
Lauterstein & Lauterstein
One Rockefeller Plaza
New York, New York 10020

CONFIDENTIAL

Dear Mr. Jacob:

As per your request, enclosed is an outline of the rationale re: study for linkage of certain Gm genotypes to chronic obstructive disease, especially, emphysema. I did some of this rationale previously; however, with the appearance of the data that the alpha1-antitrypsin genotypes are linked to the Gm genotype locus makes even more sense.

To start these studies, I think it would be beneficial to have Dr. John Vivian Wells as the Principal Investigator, since he was the first to demonstrate that a given Gm genotype was linked to height of immune response to any antigen in man. (We gave you a reprint on this; however in the event you have misplaced it, the reference is: J. V. Wells, H. H. Fudenberg and I. H. Mackay: Relation to the human antibody response to flagellin to Gm Genotypes. J. Immunol., 107:1505-1511, 1971.) As you know, some alpha1-antitrypsin genotypes which are rare are not associated with reduction of activity of the alpha1-antitrypsin. Thus, the occurrence of emphysema in these patients might merely reflect the fact that linkage of this locus to this locus to the Gm locus rather than the fact that the Pi^Z homozygotes are prone to emphysema.

Another reason for have Dr. Wells participate in this study is that he has just discovered the first human genetic marker for IgM,(J.V. Wells, J.F. Bleumers and H. H. Fudenberg: Human Anti-IgM Iso-Antibodies in Subjects with Selective IgA Deficiency. Clin. exp. Immunol., in press), and it is conceivable that if COPD or emphysema alone is due to an initial insult by a virus or other organism to which the antibody response is IgM, the same data might hold true there, i.e. the linkage is due to IgM genotype rather than IgG.

PLAINTIFF'S EXHIBIT 0531

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continued

American Medical Association Education and Research Foundation (AMA-ERF) for a major study of smoking and disease, initiated in 1964 and culminating in a final report published in 1978.[6] The industry trumpets the magnitude of its research effort by emphasizing that, "In many years, industry awards exceeded that [sic] of any government department. They have always far exceeded the smoking and health research funding of all voluntary health associations. . . ."[3] In Congressional testimony in 1982, the then-president of R.J. Reynolds Tobacco Company stated that "the tobacco industry is recognized as a leader in seeking the answers to the questions regarding smoking and health."[9]

Also illustrating the industry's use of the CTR program is a recently concluded cigarette product liability trial in Mississippi.[10] During the trial, the attorneys for the American Tobacco Company placed large charts before the jury identifying prominent universities supported by CTR grants. The attorneys emphasized that many of the supported research projects were also funded by the American Cancer Society, National Cancer Institute, and other major voluntary and governmental research-granting agencies. The tobacco attorneys specifically identified the members of the SAB by name and institutional affiliation, asking witnesses whether or not these were reputable scientists.

At no time did the attorneys state explicitly that the research at issue dealt with the health consequences of smoking; nor did they state explicitly that any of the advisors or funded scientists questioned that smoking was dangerous to health. But the intent of the tactic was clear: to establish "innocence by association," to create at least a modicum of doubt in jurors' minds that the relationship between smoking and disease (in this case, lung cancer) was definitively established; and to do so, in part, by associating the reputable SAB scientists with a search for the "as yet unknown" truth about the role of smoking in lung cancer mortality.

This courtroom experience typifies the industry's broader use of the CTR program. Mentioned nowhere in any industry public relations document is the fact that only a minority of industry-funded research addresses the relationship between smoking and health. Nor has the industry ever acknowledged that the vast majority of its funded research that *does* relate to smoking and health has identified the same disease relationships identified in tens of thousands of studies funded by other sources.[11] This includes the findings of the AMA-ERF study, which produced nearly 800 research reports and indicted smoking as a cause of lung cancer, chronic obstructive pulmonary disease, and coronary disease.[8]

To many knowledgeable observers, the tobacco industry's funding of scientific research represents an investment not in science, but rather in public relations. Thus was the conclusion of US District Court Judge H. Lee Sarokin, who presided over a prominent cigarette product liability lawsuit in New Jersey. Judge Sarokin wrote that, based on the evidence presented at trial, "the jury could reasonably conclude that the creation of [the Tobacco Industry Research Committee/Council for Tobacco Research] and the work performed was nothing but a hoax created for public relations purposes with [the industry having] no intention of seeking the truth or publishing it." He concluded, also, that there was sufficient evidence for the jury to find that "the industry . . . entered into a sophisticated conspiracy . . . organized to refute, undermine, and neutralize information coming from the scientific and medical community and, at the same time, to confuse and mislead the consuming public in an effort to encourage existing smokers to continue and new persons to commence smoking."[12]

The CTR program is part of a broader public relations campaign that has achieved notable success in misleading and deceiving the public. Survey research has consistently found that while Americans recognize smoking as hazardous to health, they greatly underestimate the dangers of smoking, both in absolute terms and relative to other health hazards.[7] In one poll, for example, lay respondents placed "not smoking" tenth among the nation's health and safety priorities. (Health professionals placed it first.) The lay respondents ranked "having smoke detectors in the home" six priorities higher in fourth position,[7] despite the fact that home fires claim about 6,000 lives per year, while cigarettes annually kill 400,000 Americans. Ironically, the most important cause of home fire deaths is the cigarette.[13]

Short of a universal rejection of CTR funding by researchers—an outcome that certainly cannot be anticipated—the scientific community has limited options with which to combat the cynical tobacco industry campaign. A clear exception, however, lies within the ready grasp of the CTR Scientific Advisory Board. Woven into the very fabric of the industry research funding process, the Board has the ability—some would say obligation—to publicly distance itself (and thereby the scientific community, which it represents in the public mind) from the industry's persistent assertion that doubt remains as to whether smoking is dangerous to health.

Is the CTR Scientific Advisory Board, through its collective silence on the health consequences of smoking, inadvertently contributing to misleading the public? A US Senator suggested this possibility nearly 30 years ago. In 1963, Senator Maurine Neuberger characterized development of the Tobacco Industry Research Committee as follows:

> The creation of the TIRC, the brainchild of [a] resourceful public relations firm . . . was a stroke of ingenuity. By offering as bait millions of dollars of sorely needed research funds, the industry was able to attract scientists of unimpeachable integrity to serve on a . . . Scientific Advisory Board. As responsible as these . . . men were, they nevertheless served the industry's purpose of associating eminent scientists with the industry position that the relationship between smoking and disease had not yet been proved.[14]

Recognizing this possibility, the Australian equivalent of the Scientific Advisory Board recently dissociated itself from the industry position, publicly and collectively. Writing in the *Medical Journal of Australia*, the panel of scientific advisors to the industry-funded Australian Tobacco Research Foundation stated, unequivocally, that

> The members of the Scientific Advisory Committee are unanimous in believing that smoking is an important causative factor in several major diseases . . . [W]e strongly endorse the view that the public should be fully informed about the risk in smokers, and we fully support any measures, which are consistent with the liberty of the individual, that are designed to reduce smoking.[15]

Clearly, there must be considerable sympathy for this scientific position within the American Scientific Advisory Board. Among the six SAB members who have individually gone on record through their responses to my query or through their published work, there is unanimous agreement that cigarette smoking causes lung cancer. But seven of their SAB colleagues have not expressed their scientific judgments through either of these vehicles, and the Board as a whole has never issued a statement about whether or not it supports the "party line" of the industry to which it provides scientific advice.

Perhaps the Board members should not be faulted for their failure to respond to my query. The message communicated to the Board members by the office of the Scientific Director of CTR may have seemed sufficiently threatening to discourage a poll response that selected Board members otherwise might have volunteered. In addition, quite independent of that communication, some members may have found my approach to this matter, or the reason for my interest, offensive, and thus decided on these grounds not to respond.

Regardless of their individual motivations, however, these scientists lend their names and credibility to a conscious tobacco industry strategy to use sponsorship of scientific research to sow doubts in the minds of the public about the dangers of cigarette smoking. As such, it might be hoped that the CTR Scientific Advisory Board would muster up the courage to take a strong public collective stand, as have their Australian colleagues, to distance themselves, as scientists, from the insidious, cynical, and misleading—and perhaps "brilliant"—public relations role played by industry funding of research. □

Acknowledgments

I am grateful to Stephen Modell for research assistance. For helpful comments on previous drafts, I thank W. Andrew Achenbaum, Fred Bookstein, Ronald M. Davis, Richard Daynard, Matthew Myers, Michael Pertschuk, Dorrie Rosenblatt, and Dinah Server. During preparation of this manuscript, I was supported in part by grant no. AG00114 from the National Institute on Aging to the Institute of Gerontology, University of Michigan.

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Editor Search Committee Seeks New Editor for American Journal of Public Health

An Editor Search Committee is actively seeking a replacement for Dr. Michel Ibrahim, who has announced his resignation as Editor of this Journal, effective January 1, 1992. The six-member search committee welcomes and solicits nominations and recommendations from the APHA membership and leadership to assist them in identifying the best available individual for this important salaried position. Nominations and statements of interest should be submitted by August 20, 1991; the committee will meet several times to consider suggestions, applications, and support materials of potential candidates.

Names of potential candidates, along with letters of endorsement and other support materials, should be sent to: Editor Search Committee, American Public Health Association, 1015 15th St., NW, Washington, DC 20005.

The following criteria will be considered by the search committee in selecting the Journal editor:

- Comprehensive knowledge and broad perspective of the field of public health, with an appreciative understanding of its many disciplines and solid grounding in the basic sciences of epidemiology and statistics;
- Professional accomplishment and identity with the public health field, including respected standing among peers, combined with an extensive network of professional contacts who can provide expertise in soliciting and evaluating materials for publication;
- Demonstrated research skills, with evidence (such as credited publication in peer reviewed journals) of firm grounding in a field of scientific inquiry within public health;
- Demonstrated writing, reviewing, and editing skills, enabling authoritative advice to authors on the suitability of prepared manuscripts, facilitating informed consideration of reviewer assessments, and equipping for the preparation of appropriate editorials as needed;
- Freedom to devote half time to editor duties;
- Working knowledge of APHA and sympathy to its advocacy goals;
- Easy access to Washington, DC;
- An institutional base is deemed highly desirable, preferably in a school of public health, a university health sciences center, or a large epidemiologic research/service organization.

APHA is an affirmative action/equal opportunity employer.

"PACK OF LIES"

A PANORAMA SPECIAL INVESTIGATION INTO THE TOBACCO INDUSTRY

A RESEARCH BRIEF

MARK KILLICK - PRODUCER
TOM MANGOLD - REPORTER
REBECCA SIMOR - RESEARCHER
JEFF GOLDBERG - U.S. RESEARCHER

INTRODUCTION

Tonight Panorama reveals what has always been suspected but never proven -- just how the tobacco industry has deliberately deceived the public for almost forty years. It's a story of commercial fraud, medical misrepresentation and the abuse of legal privilege.

Panorama's allegations are based on the tobacco industry's own internal documents and testimony from their own employees.

When the link between smoking and cancer first became known it was predicted the tobacco industry would not survive the century. In fact it's been a corporate triumph as BAT's profits showed on March 10th.

This success has been achieved by deliberately misleading the public. It was part of a brilliant defence strategy against lawsuits the industry believed could destroy it.

Tonight's programme will show:

1. How the cigarette companies tried to prevent crucial research from being published.

2. How individuals within the industry were silenced.

3. Why key labs were shut down when they seemed to be on the verge of making important new discoveries.

4. How a front organisation was established to try to give credibility to the industry's own research efforts.

5. And how the industry secretly set up a covert research organisation which organised the real medical research with a view to providing evidence and witnesses solely to help the industry fight litigation.

6. How the industry-hired lawyers slowly dominated the scientists and forced the tobacco firms to fail in their attempts to market safer cigarettes which would have saved thousands of lives.

The only man who has seen documents relating to the whole complex conspiracy calls the tobacco industry "the king of concealment and disinformation".

DOLL & WYNDER SHOCK THE INDUSTRY

The story began in 1953 when the tobacco industry was suddenly confronted with a new scientific discovery of enormous significance.

Two scientists, one British and one American, simultaneously published the first studies linking smoking with cancer. Their reports attracted massive media coverage.

The British research was carried out by Professor Richard Doll. It was statistically based and its conclusions were damning.

Doll says "When we analyzed the data we were able to conclude that smoking was emphatically a cause of lung cancer - not just that it was associated with it."

But his conservative methodology meant it was the American who attracted the lion's share of publicity.

Dr Ernest Wynder's findings were truly dramatic. He had regularly painted smoke concentrate on the backs of mice. Within a few months many of these mice developed tumours whilst the control groups remained completely healthy.

These two reports provided the first real evidence that something in tobacco smoke was extremely carcinogenic.

According to Tony van den Bergh, a senior figure in the British tobacco industry at the time, the cumulative effect was "shattering".

Nonetheless he recalls being personally told by his company chairman to challenge the evidence. "We had tame doctors who would come out and say the link was unproven. Our arguments were ridiculous. We said the correlation between smoking and lung cancer was the same as the correlation between the increase in lung cancer and the increase in the number of TV aerials".

THE TOBACCO INDUSTRY RESEARCH COMMITTEE

The US tobacco companies were also deeply concerned. They believed these two reports could actually destroy the industry. On December 15th 1953 they decided to hold a council of war at the Plaza Hotel in New York.

It was the first time since 1939 that the CEO's of all the major US tobacco companies had met together. Also present was John Hill, the chairman of Hill Knowlton - the biggest and most influential PR company in the world.

Panorama has obtained the minutes of this extraordinary meeting. The industry wanted to set up a new body called the "Tobacco Industry Committee for Public Information" which would combat the bad press caused by the scientific reports.

John Hill argued this was an insufficient response and suggested a twin track strategy of research and PR. He also suggested naming the new body the "Tobacco Industry Research Committee" which, he believed, would sound more credible to the public.

After much discussion the industry executives agreed and on January 7th 1954 the newly formed Tobacco Industry Research Committee placed full page adverts in 254 newspapers across the country.

The adverts were headed "A Frank Statement To Cigarette Smokers". They said the industry accepted "an interest in people's health as a basic responsibility, paramount to every other consideration in our business" and concluded by pledging "aid and assistance into smoking and health".

This was seen as a brilliant strategy which 'honourably' combined short term PR expediency with worthwhile long term research goals. But Ken Warner, a Michigan professor who has presented expert testimony in this area, believes it was a totally cynical manoeuvre. He says the industry were only interested in PR and had no intention of conducting any open and honest research into smoking and health.

Panorama has obtained a 1962 TIRC memo which supports Warner's view.

"The 1954 emergency was handled effectively. From this experience there arose a realisation by the tobacco industry of a public relations problem that must be solved for the self-preservation of the industry. Historically it would seem the TIRC programme has carried its fair share of the PR load in providing materials to stamp out brush fires as they rose".

THE UNACCEPTABLE ANSWERS

Nonetheless the tobacco industry did undertake a significant amount of secret research into the smoking and health question.

Panorama has obtained a number of confidential industry reports detailing this work.

Liggett & Myers commiccioned Arthur Little life sciences division to investigate the links between smoking and cancer. By 1961 their conclusions were unambiguous; "There are biological active materials present in cigarette tobacco. These are cancer causing, cancer promoting, poisonous, stimulating, pleasurable and flavourful".

Dr James Mold worked as a research scientist with Liggett & Myers for nearly thirty years. "By the early 60's we all knew that smoking caused cancer. We just weren't allowed to tell anyone".

Lorrilard had also arrived at the same conclusion. They were desperately trying to produce a safer cigarette and had even written to Dr Wynder on the subject saying "we consider your work above reproach, as usual".

British American Tobacco's response was slightly more theatrical. They became so concerned their secret research might leak out they resorted to the use of code words. Cancer became "Zephyr", mouse experiments became "Janus" experiments and other animal tests became "Conqueror" tests.

Just a few years after publishing their "Frank Statement" the tobacco industry had become less than frank with their consumers. Tony van den Burgh says the industry knew exactly what the score was. "Our products were killing people".

THE COUNCIL FOR TOBACCO RESEARCH.

By the early sixtiec the tobacco industry had evolved several parallel strategies for dealing with the smoking and health crisis. They believed the key was to pretend a debate was still raging about smoking and cancer and it was doing all it could to resolve things in an open an honest way.

To achieve this goal the Tobacco Information Research Committee was split in two; the Tobacco Institute now handled PR whilst the Council for Tobacco Research handled scientific research.

The CTR initially funded research projects examining the health hazards of smoking but they were abandoned by 1964 when the US Surgeon General published his report accepting the links between smoking and cancer.

This report made a product liability lawsuit an inevitability and the cigarette companies turned to their lawyers for help. At this moment a train of events began that would eventually lead to control of an entire industry passing to a little known Kansas City law firm.

Shook, Hardy & Bacon were specialists in product liability and they already knew the size of the problem. According to Robert Wald, a Lorillard lawyer at the time, "By 1965 David Hardy of Shook Hardy & Bacon had become the most important man in the tobacco industry".

The lawyers quickly moved into CTR. Panorama has obtained a 1965 memorandum from BAT's American subsidiary, Brown & Williamson. It shows how lawyers began deciding the thrust of CTR's research. The memo, which minutes a meeting of industry general counsel, says "Category A" proposals should be "projects of essentially adversary value". In other words projects should be prioritised which challenged the links between smoking and cancer.

The memo doesn't surprise Dr Mold. He noticed the CTR appeared to be treading water and not trying to breakthrough in key areas. He now believes CTR was always designed to fail. "CTR's policy of scattergun funding could never produce the intensive collective effort needed to resolve the industry's problems and it was probably never intended to do so".

Other documents show scientists seeking CTR funding were eventually required to write directly to the lawyers, Shook, Hardy & Bacon in Kansas City not to CTR in New York.

By 1970 there could be little doubt about the real purpose of the tobacco industry's front organisations. Despite the 1954 "Frank Statement" and many later pledges, they were for public relations not scientific research.

A 1972 memo from Fred Panzer, the Vice-President of the Tobacco Institute, reveals the industry's plan. "For twenty years the industry has operated a holding strategy consisting of creating doubt about the health charge without actually denying it".

He then says the time has come to challenge the health charge by providing some credible alternatives such as the "constitutional hypothesis". This suggested that smoking caused no ill effects and people's susceptibility to disease was determined by their individual constitutions. Panzer didn't advance any medical evidence for it but he didn't need to. It was a PR campaign not a medical debate.

It was a strategy which served the industry well. Two years later a senior Lorillard executive wrote to his CEO explaining why CTR's work was not considered important in the wider scientific community. "Historically the joint industry funded smoking and health research projects have not been selected against specific scientific goals, but rather for various purposes such as public relations, political relations, position for litigation etc. Thus, it seems obvious reviews of such programs for scientific relevance and merit in the smoking and health field are not likely to produce high ratings".

Dr Francis Roe was the research co-ordinator of the British Tobacco Research Council. He remembers visiting the CTR in 1972 and coming back with the view that it was "a distinctly shady operation". It had quickly become clear to him that the whole operation was "lawyer driven" and the research was being "deliberately constrained".

One person who the CTR tried to constrain was Dr Frederick Homburger. He had worked with them since 1954 and built up what he considered to be an open and honest relationship.

In 1973 Dr Homburger made a breakthrough. Using a sophisticated smoke inhalation machine he succeeded in inducing cancer of the larynx in 47% of a group of specially bred Syrian Golden hamsters. These results raised new warning flags about respiratory cancer induced by inhaled smoke.

The CTR were shocked by Dr Homburger's findings and immediately forbade him to publish until his work was confirmed by others. They also switched his funding from grant to contract.

A few months later Dr Dontenwill, a German professor, published the results of a similar survey he had carried out using German bred Syrian hamsters. His animals were not as susceptible to cancer as Homburger's but Dontenwill still found that 4% got cancer of the larynx.

The tobacco industry immediately dismissed Dontenwill's work as "maverick" and CTR became determined to prevent Dr Homburger from publishing. Taken together the two surveys would be dynamite.

CTR's Scientific Director, Rob Hockett, and their legal representative, Ed Jacobs, visited Dr Homburger at his Maine summer house. They told him his work had been funded on a contract not grant basis and so he did not have the right to publish. Homburger retorted that the majority of the work had, infact, been done on a grant basis.

Jacobs then told him if he published he would "never get another penny from CTR". After much wrangling they finally consented to publication providing the word "cancer" was eliminated and replaced with "pseudo epithelial hyperplasia" (pre-cancerous cells). Homburger initially accepted this distortion but changed the text back just before publication.

CTR was horrified with his report and despatched their chief press officer, Leonard Zahn, to undermine Homburger's presentation. Panorama has obtained Zahn's confidential memorandum on the events of that day.

Zahn says "I had expressed fears several weeks ago as to what Homburger might try to do with his scheduled paper...He was to have a news release with him and was to tell the press that the tobacco industry was attempting to suppress important scientific information about the harmful effects of smoking. He was to point specifically to CTR".

Zahn explained how he intended to rubbish Homburger and defend CTR at the press conference but, in the event, it wasn't necessary. Zahn managed to get the conference cancelled without Homburger knowing. He ends his memo by saying "I doubt if you or Tom will want to retain this note".

The story, however, doesn't end there. Homburger, having failed to get any publicity for his discovery, contacted Professor Dontenwill and arranged for him to repeat his allegedly "maverick" tests using the more susceptible Golden Syrian hamsters. Unfortunately Dontenwill never got the chance. The tobacco industry cancelled his funding, closed down his laboratory in Hamburg and paid him £50,000 for his silence.

Perhaps the most revealing document of all about CTR was written as late as 1980. The Vice-President of R&D at Philip Morris wrote to his counterpart at Lorillard discussing possible projects for joint industry research. He also listed the subjects to be avoided. Incredibly they included developing "new tests for carcinogenity" and attempting to "relate human disease to smoking".

CTR, as the industry never tired of reminding the public, had spent over $100 million supposedly investigating the links between smoking and health. The reality was the industry had deliberately wasted $100 million creating the illusion it was doing something. No CTR funded research was going to be allowed to undermine the industry's legal position.

THE PROBLEM LABORATORIES:

The lawyers takeover of CTR was relatively straightforward but it wasn't the only potential source of trouble. The cigarette companies own research laboratories were also capable of making damning discoveries.

The industry knew these labs could undermine their position that smoking wasn't a health hazard and made a gentleman's agreement to restrict internal biological research. However this was increasingly ignored by companies terrified of being left behind in a competitive marketplace.

The American Tobacco Company had built a new facility at Bermuda Hundred which had several animal rooms (including one for dogs) as well as an autopsy room. Liggett & Myers had expanded their work with Arthur Little's life sciences division and BAT had substantially upgraded its facilities in England and Germany.

But the most important internal work was being done in Winston, Salem where RJR had built a state of the art laboratory nicknamed "the mouse house". They had also developed a pioneering machine that forced animals to breathe smoke eight hours a day.

Dr Antony Colucci was one of the project managers at the time and he recalls one particularly exciting project that was starting to show just how smoking caused emphysema. Colucci's colleague was Joe Bumgarner who says "we weren't quite there but it was potentially great work".

The lawyers didn't see it that way. To them the labs were time bombs ticking away at the very heart of the industry and they decided to defuse them.

Panorama has obtained a 1970 letter from David Hardy of Shook, Hardy and Bacon to BAT's US subsidiary which explains in detail why the lawyers had become so concerned about the consequences of this type of research.

He says "In our opinion the effect of testimony by employees or documentary evidence from the files of either BAT or B&W which seem to acknowledge or tacitly admit that cigarettes cause cancer or other diseases would likely to be fatal to the defence of either or both companies in a smoking and health case".

He goes on to say "It could even be the basis for an assessment of punitive damages if it were deemed a reckless disregard for the health of a smoker".

This is one of the most important documents ever extracted from the tobacco industry. It spells out their real agenda. The lawyers were more worried about protecting the industry than

researching into smokers' health.

Their view was soon translated into action.

In December 1970 RJR's mouse house was shut down, the workers sacked and their notebooks collected by the legal department. Bumgarner has no doubts as to the reason why. He recalls being told "the Surgeon General is cutting our throats. We don't need to do it ourselves".

After Bumgarner and the others left, several strange events occurred. One of the key experiments had involved keeping a group of rabbits alive during a three year smoke inhalation study. According to Bruce Cooke, an Illinois lawyer who has studied these events, the rabbits were expected to yield unique information on the effects of smoke on living tissue. However soon after the mouse house was shut the rabbits simply disappeared. The company can offer no explanation.

Almost as mysterious was the role of Dr Frank Colby. He was brought in to examine the scientist's research notes. A secretary remembers him reading the documents and then shredding most of them. Again the company can offer no explanation.

The biggest British laboratory was at Harrogate. It was jointly funded by a number of UK tobacco companies through the British Tobacco Research Council. Peter Lee was employed there as a senior scientist. He remains a consultant to the tobacco industry.

Lee says Harrogate's work with animals failed to prove or disprove a connection between smoking and ill health. However it did become apparent that this research route was running into a cul de sac. Harrogate was closed down in 1974 and suprisingly the TRC abandoned its research role. Lee has admitted on camera that he himself was convinced of the association between smoking and ill health, and that the epidemiological work being conducted at the time was pretty conclusive. He also admits that the industry lawyers were around to ensure inter alia, that employees did not say things the industry might later regret.

BAT, the largest tobacco company, continued to do internal research work at their laboratories in Southampton. But conditions were difficult and the publication of results strictly controlled. Studies were labelled: "Must Not Be Shown to Unauthorised Personnel."

Dr James Green was their Director of Research. He became increasingly disillusioned as he fought to publicise many of their findings. In a memo to himself he wrote: "the position of the tobacco companies is dominated by legal considerations....it has retreated behind impossible, perhaps ridiculous, demands for what in PR terms is called scientific proof..usually the first

reaction of the guilty".

His widow, Olwyn Green, recalls the increasingly bitter fights between her husband and the BATCO board. "They simply ignored what he told them".

In 1980 Dr Green finally resigned and went public. He told Panorama: "I believe that smoking can cause harm. I'm quite sure it can and does. Infact I quite sure it's a major factor in lung cancer in our society". Shortly afterwards BAT abandoned all research into smoking and health.

The legal domination of the industry had placed the PR company, Hill Knowlton, in an impossible position. The Tobacco Institute continued to place advertisements saying they were actively investigating the effects of smoking on health but the PR professionals knew the truth. The original "Frank Statement" strategy was a sham.

Hill Knowlton argued fiercely that a better way for the industry to proceed was to concede the old products may have some potential health risks and to swiftly introduce new safer cigarettes. This would have the advantage of being honest and might even win back smokers who had quit.

However the lawyers would have none of it. Their view was the industry should tough it out. No concessions and no safer cigarettes.

In 1970 Hill Knowlton resigned the entire tobacco industry account. Loet Velmans recalls the final months. "Everyone was frustrated. The lawyers just would not consider any other strategy".

THE SAFER CIGARETTE:

The development of a safer cigarette had long been an industry option. Filter and low tar cigarettes were first introduced in the 1950's and initially advertised as being safer. Then the lawyers realised these claims implied other products were less safe and began insisting on euphemisms like "kinder on your throat" and "milder".

These legal concerns were to doy the industry for the next thirty years undermining any attempt to develop a genuinely safer cigarette.

One such attempt was made by BAT in the 1970's with the introduction of "Non Tobacco Materials". NTM was a less complex material and less harmful than tobacco.

Panorama has obtained a copy of a legal opinion about NTM given to BAT in 1976.

The barrister said that "All assertions that NTM is safe (or even safer) should be avoided, not least because of the subsidiary implication that Tobacco is not safe (or less safe)".

This advice prevented BAT from marketing NTM in a way that would appeal to the consumer and, coupled with the government's refusal to give NTM a tax advantage over tobacco, meant NTM could never became a viable product.

Another attempt to produce a safer cigarette was made by Ligget & Myers. They spent twenty years developing "Tame" - a cigarette with a revolutionary Palladium catalyst. This catalyst destroyed one of the major cancer causing ingredients in smoke.

It's inventor was Dr James Mold. He says the Palladium catalyst would have saved "thousands of lives". But it was never marketed. One reason was the continued hostility of Ligget & Myer's lawyers to the whole project.

The most serious attempt to manufacture a safer cigarette was made by RJ Reynolds in 1988. They spent $300 million developing a revolutionary new product called "Premier." It looked like a cigarette but could more accurately be described as a nicotine delivery system.

Premier didn't burn tobacco - it heated it. This meant much of the materials present in conventional cigarette smoke were not present in Premier. It really was a major breakthrough.

Shook, Hardy and Bacon, the industry's lawyers, didn't see it in those terms. Panorama has obtained a memo from them commenting on Premier. They were very concerned that it "may threaten current litigation strategy".

They warned that Reynolds' new product "concedes certain shortcomings of their existing products" and repeated their view that "the development of this product may have significant effects on the tobacco industry's joint defence efforts".

Premier was pulled off the market three months after it had been launched. Dr Hoffman of the American Health Foundation believes "thousands of lives would have been saved if these modified cigarettes had been properly marketed".

Panorama has discovered that at least four safer cigarette patents have been filed with the US Patents Office in the last three years. None have gone into production.

SPECIAL PROJECTS:

The industry's biggest secret only came to light last year when a US judge published a remarkable legal opinion.

In 1988 Judge Lee Sarokin presided over the Cipollone case, the only tobacco liability case the industry did not initially win.

Last year Sarokin was preparing to hear his second tobacco case when he was asked to rule on the admissibility of a number of industry documents. He read a sample selection and concluded "the tobacco industry may be the king of concealment and disinformation". Sarokin had uncovered the industry's innermost secret. Shortly afterwards he was removed from the case.

Sarokin had found out CTR had never abandoned research into the hazards of smoking but had simply transferred it in their "Special Projects" division where they could maintain direct control over the work. At the lawyer's whim, research in this division could be kept completely confidential, commissioned solely on a contract basis and organised directly by lawyers thus making it attorney/client privileged. A protective shield had been constructed by the lawyers to keep damaging research from disclosure. We have discovered that Special Projects worked secretly from a tenth floor office at the CTR building in New York, where they ran one of the biggest computer centres then in the US. We plan to interview a rare primary source on this revelatory subject.

Given the publicity attached to the "Frank Statement" and the repeated pledge to inform the consumer, Sarokin believed the public had a right to know about special projects. He also believed that many of the tobacco liability lawsuits would have had a different outcome had their research been published.

Sarokin argued that claiming this material was attorney/client privileged was an abuse of the law and the lawyers should be subject to a criminal prosecution. He told Panorama (on a background basis) documents showed the fraud was orchestrated by Shook, Hardy and Bacon.
Ken Warner has studied a list of Special Projects briefs. He was astounded. "Special Projects was at the forefront of tobacco health research. I had no idea the industry was doing such state of the art work".

One of the key players in Special Projects was Dr Frank Colby, the former Reynolds scientist. He gave a deposition saying he was "a person wearing two hats. No 1, he was a person in charge of R&D information; No 2, he was responsive to the legal dept".

A few years earlier Colby had explained the way "Special Projects" worked to Dr John Slade, a professor at the Robert Wood Johnson Medical School.

Slade was reviewing a CTR publication dealing with the chronic exposure of mice to cigarette smoke and he was puzzled. The book's conclusions supported the industry but it was controversial work of a type not usually done by CTR.

Slade contacted Colby and asked him to lunch. Colby explained the project had originally been commissioned by Special Projects but when the conclusions had come out so favourably for the industry it was decided to transfer the book to CTR. "Don't expect too many others" joked Colby as the lunch ended.

Colby's short explanation provides the only insight into Special Projects yet given to the outside world. However more information may come out soon - the Brooklyn DA's office has launched a criminal investigation into CTR's Special Projects.

CONCLUSION:

Judge Sarokin has identified the fundamental issues in this story which concern the relationship between big business and the public. In his opinion he writes "all too often in the choice between the physical health of consumers and the financial well being of business, concealment is chosen over disclosure, sales over safety and money over morality".

Panorama's revelations will only add to his concerns. As the industry's profits continue to rise; as the cigarette salesmen move into the unsuspecting third world; as a new generation of gullible youngsters in Britain and throughout the West take up the smoking habit for the first time, the duplicity of the tobacco industry is brought to light. It has already cost the lives of millions of people who bought their pack of lies.

PLEASE NOTE: THIS IS AN INITIAL RESEARCH BRIEF ONLY.
ALL MATERIAL MUST BE CHECKED PRIOR TO TRANSMISSION.

Exhibit 18

THE UNIVERSITY OF TEXAS SYSTEM
CANCER CENTER
Texas Medical Center Houston, Texas 77030

June 27, 1977

Mr. Don Hoel
Shook Hardy & Bacon
20th Floor-Mercantile Bank Tower
1101 Walnut
Kansas City, Missouri 64106

CONFIDENTIAL

Dear Don:

Enclosed is a budget to enable us to complete the volume on the environmental factors and each cause of death, some important aspects of which I reported at the Maxwell Conference as they pertain to lung cancer, and the textbook on epidemiology which the publishing company has suggested be written as a second volume to the 700 page incidence of cancer reference book, which will be published in October by the Raven Press. The Clayton Foundation enabled us to continue our staff from June 1 and will carry us through September, 1977.

Mr. Maxwell wrote me a letter saying how much they enjoyed the talk and especially the question period and said that if I had been the only speaker they would have enjoyed asking questions for the whole three hours. I missed you and Alex.

This is my revised budget to go with the report I submitted earlier.

Sincerely,

Eleanor J. Macdonald
Professor of Epidemiology
Department of Epidemiology

EJM:eh
enc.

Budget Request
October, 1977-September, 1978

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Biometrician (50%)	$ 12,000	
Assistant Epidemiologist (100%)	14,865	
Assistant Epidemiologist (100%)	14,865	
Secretary (100%)	10,495	
Programmer (33%)	6,451	
Systems Analyst (Consultant as needed)	3,500	
Subtotal		62,176
Computer Time	4,800	
Consumable Supplies	1,000	
Travel	3,000	
Fringe Benefits (Salaries)	6,218	
Subtotal		15,018
Subtotal		77,194
15% Overhead		11,579
TOTAL		88,773

June, 1977

CONFIDENTIAL

WASHINGTON UNIVERSITY
SCHOOL OF MEDICINE
ST. LOUIS, MISSOURI 63110

JOSEPH H. OGURA, M.D.
CLINICAL PROFESSOR AND HEAD
DEPARTMENT OF OTOLARYNGOLOGY

BARNES HOSPITAL
3600 KINGSHIGHWAY

June 10, 1974

Mr. William W. Shinn
Shook, Hardy & Bacon
915 Grand Avenue
Kansas City, Missouri 64106

Dear Mr. Shinn:

This is a request for support of a planning grant for nasopulmonary research preparatory to submission of a formal proposal on the effects of tobacco and air pollutants on the lung.

I am submitting a curriculum vitae for myself and Dr. Kawamoto, whom I am most anxious to keep as he is a fine person and has done outstanding work in our nasopulmonary research.

I am requesting the amount of $24,000 for one year, as we will need financial support prior to submission of a long range proposal. I would like to hear from you by the middle of July if possible.

Very sincerely yours,

Joseph H. Ogura, M.D.

JHO/sas

Yale University New Haven, Connecticut

SCHOOL OF MEDICINE
333 Cedar Street
Department of Internal Medicine

November 23, 1965

CONFIDENTIAL

Edwin J. Jacob
Cahall Madinger Forsyth & Zacker
51 West 51st Street
Rockefeller Center
New York, N. Y. 10019

Dear Ed:

I am writing this letter to describe (briefly, as you requested) the research for which I shall probably need support for the period from January 1 to June 30, 1966. The amount needed is $ 5595, which includes $ 3008 for a research assistant with a MPH degree, who is actively working on the data of cancer of the larynx; $ 2387 for a secretarial assistant; and $ 200 for miscellaneous supplies.

The research consists of intensive studies of the natural course and post-therapeutic outcome of three different cancers: lung, rectum, and larynx. We have worked out special new techniques for processing a great deal of the complex clinical and personal data that have hitherto been omitted from most existing studies of cancer——mainly because the data were regarded as too complex to be managed and analyzed. Using principles of "clinical taxonomy", symbolic logic, and set theory, we have worked out the techniques for identifying, classifying, and analyzing many "variables" that have hitherto been ignored. The results of our current analyses have brought considerable clarification to a number of issues that have hitherto been regarded as controversial or impossible to analyze——because no one has really hitherto worked out a way to analyze them effectively. With the new techniques, we have organized the data in a form where they can now be stored in a computer, analyzed even more intensively, and made available for practical use in future appraisals of etiology, prognosis, and therapy.

In addition, we have obtained a great deal of new data on the relationship of cigarette smoking to the course and biologic behavior, rather than the cause, of these three cancers. If cigarette smoking is as harmful as has been alleged, it should not only "cause" these diseases but should also make their manifestations and outcome worse in people who were smokers. Yet, in the informal analyses we have done so far, no such clinical effects have been noted. The manifestations and course of the diseases do not appear to be positively correlated with the amount, if any, of cigarette smoking in the affected patients. Our enumerated analysis of these data has hitherto been informal, however, and I now

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want to computerize the results for a more precise appraisal. We now have such intensive data for about 1200 patients with these three cancers, and the use of a computer is desirable for the analyses.

The main need in this type of work is trained human personnel to assist in the painstaking, arduous task of reviewing records, confirming facts, and coding data. From funds made available to me by the West Haven VA Hospital, I shall have support for two people who have currently been working on this project. The work really requires at least two more people, however, and the funds I am looking for will be to support those other two people.

I currently have placed grant applications with two different agencies that will announce their decisions in mid-December. Should both agencies reject the applications——a strong possibility in this era when no one seems to want to support clinical research——I shall need the help I have cited until I can compose additional new grant applications to other agencies for support after June 30, 1966.

If you want reprints, further descriptions, or any other information about this matter, please let me know. I shall be most grateful for any help you and your colleagues can provide.

Sincerely yours,

Alvan R. Feinstein, M. D.
Associate Professor of Medicine

ARF/lp

CONFIDENTIAL

University of Hawaii at Manoa

Behavioral Biology Laboratory
Pacific Biomedical Research Center
Snyder Hall 115 • 2538 The Mall • Honolulu, Hawaii 96822
Telephone: 948-8955

April 11, 1975

Mr. Edwin J. Jacob
Jacob & Medinger
1270 Avenue of the Americas
Rockefeller Plaza
New York, N.Y. 10020

Dear Ed:

This letter is for the purpose of recording the essential features of our recent telephone conversations concerning the funding and operation of the pending research program on genetics and tobacco-related behaviors.

It has been agreed by the investigators that I should serve as coordinating investigator. In this role, I would serve as the communication link between the investigators and the granting consortium. I would be responsible for coordinating the preparation and submittal of required fiscal and scientific progress reports and arranging for periodic meetings of the consulting and review panel.

Responsibility for the scientific conduct of the research would be assumed by the principal investigators of the three separate projects, as follows:

Hawaii study -- Geoffrey Ashton

Half sib-twin study -- Wilson Crumpacker and
Steven Vandenberg

Animal study -- Gerald E. McClearn

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The principal investigators would be responsible for expenditures on their particular projects, and would have freedom to transfer funds among budget categories as required. With mutual consent of the principal investigators involved, funds could be transferred between projects. However, all expenditures would be made in compliance with the applicable state and University rules of Colorado or Hawaii, as relevant.

The consulting and review panel will be composed of scientists mutually acceptable to the investigators and to Dr. William Gardner. After a period of approximately 18 months, a meeting of the consulting and review panel will be convened to evaluate progress of the projects and to make recommendations to the grantors concerning continuation of support. In the case of a recommendation to discontinue a project, funds for phasing out the operations will be continued at least in amount sufficient to meet staff personnel obligations for a period up to an additional six months, depending on the terms of employment.

Assuming that obligations have been undertaken to employ staff through the full second year, the amount of savings from the second year budget that would be made by termination of data collection and analysis after 18 months would be approximately as follows:

Hawaii study -- $82,076

Half sib-twin study -- $50,737

Animal study -- $27,268

If obligations are undertaken only to provide 60-day notice of termination of employment, then additional savings in the amounts of $7,400, $5,000 and $40,000, respectively might be made.

If the circumstances are such as to warrant a continuation of data collection and analysis during the phase out period, a negotiated amount not to exceed the budgeted amount for the next six months, but with a longer time limit for expenditure, will be made available.

In the event of favorable recommendation at the time of evaluation, research support will be continued, and a second evaluation meeting will be held approximately at the end of 27 months. The purpose of this meeting will be to evaluate progress and to make recommendations regarding funding for the fourth and fifth years of the study.

I am anxious to know if the above is an accurate summary of the principal points of our discussions.

Sincerely,

Gerald E. McClearn

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

BERKELEY · DAVIS · IRVINE · LOS ANGELES · RIVERSIDE · SAN DIEGO · SAN FRANCISCO · SANTA BARBARA · SANTA CRUZ

SAN FRANCISCO, CALIFORNIA 94122

SCHOOL OF MEDICINE
DEPARTMENT OF MEDICINE

Direct: (415) 666-1711

Section of Hematology and Immunology

July 20, 1972

Mr. Edwin Jacob
Lauterstein & Lauterstein
One Rockefeller Plaza
New York, New York 10020

CONFIDENTIAL

Dear Mr. Jacob:

As per your request, enclosed is an outline of the rationale re: study for linkage of certain Gm genotypes to chronic obstructive disease, especially, emphysema. I did some of this rationale previously; however, with the appearance of the data that the alpha1-antitrypsin genotypes are linked to the Gm genotype locus makes even more sense.

To start these studies, I think it would be beneficial to have Dr. John Vivian Wells as the Principal Investigator, since he was the first to demonstrate that a given Gm genotype was linked to height of immune response to any antigen in man. (We gave you a reprint on this; however in the event you have misplaced it, the reference is: J. V. Wells, H. H. Fudenberg and I. R. Mackay: Relation to the human antibody response to flagellin to Gm Genotypes. J. Immunol., 107:1505-1511, 1971.) As you know, somealpha1-antitrypsin genotypes which are rare are not associated with reduction of activity of the alpha1-antitrypsin. Thus, the occurrence of emphysema in these patients might merely reflect the fact that linkage of this locus to this locus to the Gm locus rather than the fact that the Pi^z homozygotes are prone to emphysema.

Another reason for have Dr. Wells participate in this study is that he has just discovered the first human genetic marker for IgM,(J.V. Wells, J.F. Bleumers and H. H. Fudenberg: Human Anti-IgM Iso-Antibodies in Subjects with Selective IgA Deficiency. Clin. exp. Immunol., in press), and it is conceivable that if COPD or emphysema alone is due to an initial insult by a virus or other organism to which the antibody response is IgM, the same data might hold true there, i.e. the linkage is due to IgM genotype rather than IgG.

PLAINTIFF'S EXHIBIT 0531

0120476

continued

CONFIDENTIAL

Due to the fact that Dr. Wells is an M.D., Ph.D., and starting salary for Assistant Professor of Medicine at the University of California (including fringe benefits) is approximately $25,000 per year, and since we have found it is much easier for a trained physician (especially a faculty member) to obtain cooperation from the various pulmonary specialists here, Kaiser Hospital and other institutions in the Bay Area, I think it would be much more effective to provide funds for Dr. Wells than simply for a postdoc.

Further, we would test for many more Gm factors than originally presented, i.e. not only the major five or six, but perhaps 20. Dr. Wells would also require about $5,000 for supplies. Therefore, the total amount would be $30,000 for one year. If we get results during this time, we could put in for a NIH grant for pursue this further and perhaps shift our allocations from the AMA-ERF grant in part for this purpose, since alpha$_1$-antitrypsin genotype characterization by the Fagerhol method would be part of the project. We are equipped to do this.

As you are aware, Dr. Wells has been offered an Associate Professor position elsewhere, and must make a decision by September 1; therefore, an early reply would be greatly appreciated. Please let us know if you are interested. Dr. Wells would prefer staying here if funds can be arranged.

Thank you.

Very sincerely,

H. Hugh Fudenberg, M. D.
Professor of Medicine, UC, San Francisco
Professor of Bacteriology and Immunology, UC, Berkeley
HHF/sw

Encl. Outline of Rationale

Exhibit 19

Public Health Policy Forum

Tobacco Industry Scientific Advisors: Serving Society or Selling Cigarettes?

Kenneth E. Warner, PhD

ABSTRACT

According to industry documents, the tobacco industry has executed a "brilliantly conceived" strategy to "creat[e] doubt" in the public's mind about whether cigarette smoking is in fact a serious cause of disease. A component of this strategy has been the funding of scientific research "into the gaps in knowledge in the smoking controversy." Grant review and selection are performed by a group of independent scientists. Knowledgeable observers believe that the existence of this research funding program in general, and the Scientific Advisory Board in particular, is intended by the industry to reinforce doubts in the public mind about the severity of the hazards posed by smoking. Because the Advisory Board has never taken a public stance against the industry's position that the causal relationship between smoking and disease remains unproven, I polled these scientists to determine whether they believed that smoking is a cause of lung cancer. Despite repeated opportunities, only four of 13 board members responded, all affirmatively; two others have expressed their judgment that smoking causes lung cancer in their professional publications. Thus, over half of the Board members, and the Board as a whole, have not gone on record as rejecting the industry's "party line." It might be hoped that the American scientists would follow the lead of the members of a similar body of scientists in Australia who have taken a strong and public stand against the industry position that smoking is not an established cause of disease. (*Am J Public Health.* 1991;81:839–842)

Introduction

For nearly 40 years, the tobacco industry has maintained that cigarette smoking has not been proven to be a cause of any disease. In what a vice president of the Tobacco Institute characterized as a "brilliantly conceived and executed" strategy, the industry has consciously striven to "creat[e] doubt about the health charge without actually denying it."[1] Tactics have ranged from attempts to define the smoking-and-health lexicon for social discourse (referring repeatedly, for example, to a scientific "debate" about the smoking-and-health "controversy") to publicly distorting the findings of scientific studies linking smoking to disease.[2]

Another tactic has involved direct sponsorship of biomedical research to lend credibility to the industry's claim that it "remains committed to advancing scientific inquiry into the gaps in knowledge in the smoking controversy."[3] Toward this end, in 1954 the industry formed the Tobacco Industry Research Committee (TIRC), renamed the Council for Tobacco Research-U.S.A. (CTR) in 1964, "to provide financial support for research by independent scientists into tobacco use and health."[4]

The public was introduced to this program in early January 1954 in a full-page advertisement run in 448 newspapers in 258 cities, reaching an estimated 43 million Americans. Entitled "A Frank Statement to Cigarette Smokers," the ad said that the industry would sponsor impartial scientific studies on the relationship between smoking and health and would "let the results speak for themselves." The ad assured readers that the tobacco companies "accept an interest in people's health as a basic responsibility, paramount to any other consideration in our business . . . We always have and always will cooperate with those whose task it is to safeguard the public health."[5]

Readers of the *Journal* need no assistance in evaluating the sincerity of that "frank statement." More than 30 years later, the industry continues to use this sponsorship of research to attempt to create the impression of "scientific controversy," and of the industry's "well-intentioned commitment" to "resolving" the "controversy." This is demonstrated in the following statement from a 1986 publication of the Tobacco Institute:

> Industry support of independent research is in excess of $130 million and has resulted in publication of nearly 2,600 scientific papers. *Eminent scientists believe that questions relating to smoking and health are unresolved.* (emphasis added) and the tobacco industry will make new commitments to help seek answers to those questions.[4]

While the individual components of this statement are literally accurate, the intent and effect of their wording and their juxtaposition are to mislead. The statement implies that the industry's grants support research directed at resolving "questions relating to smoking and health." In the main, this is simply not true. Most CTR-funded grants support biomedical research not related to the health consequences of smoking. In a recent survey of principal investigators funded by CTR grants in 1989, almost 80 percent of respondents indicated that none of their research, current or past,

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examined the health effects of smoking.[6] Furthermore, the vast majority of industry-supported research that has addressed the health effects of smoking has produced findings consistent with the Surgeon General's conclusion that smoking is a major cause of numerous diseases."[3,8]

The second sentence of the Tobacco Institute's statement might readily be interpreted to mean that eminent scientists question whether smoking causes disease. While scientists do have questions about the specific mechanisms of causality, there is virtually no disagreement that smoking is a major cause of disease. In the above-mentioned survey of CTR grant recipients, for example, over 90 percent of the respondents concurred with each of the following: "most deaths from lung cancer are caused by smoking"; "smoke from someone else's cigarette is harmful to a non-smoker"; and "cigarette smoking is addictive."[6]

In addition to distorting reality in its printed matter disseminated to the public, the tobacco industry has appealed to its ongoing "commit[ment] to advancing scientific inquiry into the gaps in knowledge in the smoking controversy" in dealing with the media, in presenting congressional testimony, and in defending itself in court against charges of product liability. Examples are noted below.

The industry's use of the CTR grant program raises a number of difficult and troubling questions, including the following: Should scientists directly lend their credibility to the industry by serving as members of its Scientific Advisory Board, the body of independent scientists who perform grant review and selection? As either advisors or recipients of funding, what obligations, if any, do scientists have to the larger society as a result of their involvement in the CTR process? For example, do they have a moral obligation to publicly state their disagreement with the tobacco industry's position that smoking has never been proven to be a cause of any disease? At a purely pragmatic level, does the scientific knowledge generated by CTR-funded research produce social benefits that outweigh the costs of the industry's deceptive public relations use of the process? At the most fundamental level, should researchers accept financial support from an industry that annually knowingly causes the deaths of some 400,000 Americans?[7]

These questions could be the subject of a detailed treatise in the general domain of the ethics of science. I leave that task to others. Rather, my purpose in this paper is simply to relate, and put into context, the saga of my attempt to poll the members of the Scientific Advisory Board to determine whether or not they believe that smoking causes lung cancer. The experience offers lessons to those who might wish to tackle the more formidable assignment of an ethical analysis of scientists' involvement in tobacco industry-funded research.

Poll Process and Results

Elements of the public might be led by industry statements such as that quoted above to infer that the CTR's Scientific Advisory Board (SAB), representing the broader biomedical science community, shares the industry's "uncertainty" about whether smoking is a true health hazard. Because, as a body, the SAB has never gone on record as rejecting the tobacco industry's position, I wrote to each Board member on August 4, 1987 asking for a yes or no response to the following question:

> Do you believe that cigarette smoking causes lung cancer? In answering this question, interpret causality in its lay public meaning. You should respond in the affirmative if you believe that smoking, or any of the components of cigarette smoke, either initiates or promotes lung cancer.

I restricted the question to a single disease to make the question specific and to have it address the smoking-related disease the public most fears and most strongly associates with smoking. In addition, the vast body of evidence indicting smoking as a cause of lung cancer is uncontroverted and of long standing.[7]

The 13 Board members were assured anonymity. Two promptly returned affirmative responses through the mail. One other responded affirmatively by phone within a week of the mailing. A fourth responded affirmatively in early September 1987. Of the remaining nine Board members, six refused in writing or by phone to respond to the question; the other three could not be reached following three written communications and repeated phone calls.

To ascertain whether Board members had discussed the relationship between smoking and lung cancer in their professional writing, a MEDLINE literature search was undertaken. The search revealed that two Board members who had declined to answer my inquiry had published their scientific judgment that smoking causes lung cancer. Two of the affirmative respondents to the poll were also identified as having adopted this position in writing. Consequently, between their direct poll responses and published work, six of the 13 Board members have agreed explicitly that smoking causes lung cancer. Of the remaining seven Board members, none was found to have taken a position on this issue in his published work. Typically, this reflected the fact that the scientist's work had not involved lung cancer.

The response rate to the poll may have been influenced by a communication to each Board member from the office of the Scientific Director of CTR informing the Board that I had been listed as an expert witness in three tobacco product liability lawsuits, including one in which CTR was named as a party. Thereafter, two additional letters to Board members and follow-up phone calls produced no more poll responses, despite renewed assurances of anonymity.* One Board member, who had responded to the poll previously, said, "I don't think there's a guy on that [Board] who doesn't believe that cigarette smoking contributes to an increased risk of lung cancer . . . [W]ithin the ordinary use of language, you've got to say that smoking causes lung cancer." He explained, however, his belief that the members of the Scientific Advisory Board were "terrified" (his word) of involvement in tobacco product liability lawsuits. He lamented a state of affairs in which reputable, well-intentioned scientists would not acknowledge that they believed that smoking causes lung cancer.**

A Broader Context

In the three and a half decades since its formation, the Council for Tobacco Research (and its predecessor, TIRC) has contributed many millions of dollars to research. CTR served as the tobacco industry's liaison on a $15 million award from the six principal tobacco companies to the

*In the final letter, I informed the Board members that the one trial (not three) for which I had agreed to serve as an expert witness had been completed, the case had not included CTR as a party, and I was not called upon to testify. Subsequently, the first trial was declared a mistrial. I testified at the retrial on September 11, 1990. My testimony did not include mention of this poll.

**Consistent with this Board member's assessment was a phone conversation with another Board member. Each of approximately 20 questions I asked elicited the unvarying reply: "May I just thank you for calling?" He refused to explain why he would not respond to the poll.

Budget Request
October, 1977-September, 1978

Biometrician (50%)	$ 12,000	
Assistant Epidemiologist (100%)	14,865	
Assistant Epidemiologist (100%)	14,865	
Secretary (100%)	10,495	
Programmer (33%)	6,451	
Systems Analyst (Consultant as needed)	3,500	
Subtotal		62,176
Computer Time	4,800	
Consumable Supplies	1,000	
Travel	3,000	
Fringe Benefits (Salaries)	6,218	
Subtotal		15,018
Subtotal		77,194
15% Overhead		11,579
TOTAL		88,773

June, 1977

Exhibit 20

What Scientists Funded by the Tobacco Industry Believe About the Hazards of Cigarette Smoking

K. Michael Cummings, PhD, MPH, Russell Sciandra, MA, Amy Gingrass, and Ronald Davis, MD

ABSTRACT

Despite overwhelming evidence documenting the hazards of cigarette smoking, the tobacco industry denies that smoking has been proven to cause disease. The industry professes a desire to clear up the smoking and health "question" and often points to its support of the Council for Tobacco Research (CTR) as evidence of its interest in investigating the health dangers of smoking. This paper presents results of a survey of CTR-funded scientists regarding their beliefs about the health dangers posed by smoking cigarettes. The vast majority of scientists funded by the CTR believe that cigarette smoking is an addiction that causes a wide range of serious, often fatal, diseases. This result suggests that the tobacco industry is unwilling to accept even the opinions of scientists it has deemed worthy of funding. Scientists should consider the ethical implications of accepting funds from the CTR and other tobacco industry-supported institutions. (*Am J Public Health*. 1991;81:894–896)

Introduction

The US Surgeon General has stated that "smoking represents the most extensively documented cause of disease ever investigated in the history of biomedical research."[1] Despite overwhelming scientific evidence against cigarettes, the tobacco industry continues to assert that controversy, debate, and uncertainty exist among scientists concerning smoking as an important cause of illness.[2–4]

In 1972, a confidential memorandum from a Tobacco Institute (TI) vice-president described TI policy as "creating doubt about the health charge without denying it, advocating the public's right to smoke without actually urging them to take up the practice, and encouraging objective scientific research as the only way to resolve the question of the health hazard."[5] Industry spokespersons often point to the industry's support of the Council for Tobacco Research (CTR) as evidence of corporate interest in obtaining scientific evidence on the "alleged" relationship between tobacco use and disease.[3]

The CTR, formed in 1954 by cigarette manufacturers, describes its primary mission as support of research into questions of tobacco use and health.[6] The council awards peer-reviewed research grants to independent scientists who are assured complete scientific freedom in conducting and publishing their studies. Since 1954, the council has provided more than $150 million for 1,108 original studies by more than 700 scientists.[6] In 1989, the CTR listed 204 active projects.

We present results of a survey of CTR-funded investigators, which characterizes what the investigators believe regarding the health effects of tobacco.

Methods and Materials

The study population included the principal investigators of research projects funded by the CTR in 1989.[6] Of 204 investigators listed, 179 were located at universities or institutions in the United States. This survey was restricted to those working in the United States.

Eligible survey participants were mailed a one-page questionnaire assessing their beliefs about the relation between cigarette smoking and various health complications and asking them to rank the importance of 10 different areas of tobacco research. Respondents were asked about their current and past research on tobacco and their cigarette smoking status. A cover letter stated that we were surveying "scientists who had published studies on smoking and health and/or have received research support from organizations interested in the tobacco and health issue."

Of 179 questionnaires mailed to eligible scientists in July 1990, 13 were returned with an incorrect mailing address. A total of 77 completed questionnaires were returned, which represents a response rate of 46% (77/166). No further attempt was made to elicit response. A comparison of responders and nonresponders revealed no significant differences in academic credentials (PhD vs MD), institutional affiliation (university vs other), or the nature of the CTR-funded project (i.e., a tobacco study vs a nontobacco study).

Results

Respondents were asked to "indicate the degree to which you believe the scientific evidence suggests a causal relationship with cigarette smoking" for

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This paper was submitted to the journal October 29, 1990, and accepted with revisions March 6, 1991.

eight separate health complications. With the exception of bladder cancer, nearly all respondents rated the relationship between smoking and illness as "strong" or "moderate" (Table 1). Only 1 of 77 respondents was a current smoker. Nationally, approximately 29% of adults smoke.[7]

Only 22% of respondents indicated that any of their current or past research focused on the health effects of tobacco use.

Ninety-four percent of respondents agreed with the statement "smoke from someone else's cigarette is harmful to a nonsmoker"; 91% agreed that most deaths from lung cancer are caused by smoking; and 76 of 77 agreed with the statement "cigarette smoking is addictive" (Table 2).

Rankings of the importance of 10 areas of research on tobacco varied widely (Table 3). Overall, research on preventing tobacco use received the highest ranking, followed by smoking cessation methods.

Discussion

The low response rate is not unusual for a mailed questionnaire survey,[8] but does potentially limit the generalizability of the findings. The comparison of respondent and nonrespondent characteristics does not suggest any systematic response bias. It is possible that among those not responding to the survey were some who feared retribution from the tobacco industry. Such fear, if it existed, would likely be among those whose views are congruent with the majority of the respondents. It is also possible that those with less scientifically acceptable positions or greater commitment to the tobacco industry were less likely to respond, though it would seem to be in the industry's interest to have its views represented in such a survey, if possible. For these reasons, we believe the results accurately represent views of scientists funded by the CTR.

The survey shows that most scientists funded by the CTR believe cigarette smoking is an addiction that causes a wide range of serious, often fatal, diseases. This finding conflicts with the tobacco industry's description of the scientific community as divided on the question and indicates the industry does not accept the opinions even of scientists whose research it funds. Although acknowledging a need for additional investigation of the mechanisms linking smoking and disease, respondents gave the highest priority to research on tobacco use prevention and cessation. None of CTR's active research projects relate to these topics. Despite its stated mission to fund research into the etiology of diseases "alleged" to be related to tobacco use, only 1 in 6 CTR-funded scientists reported conducting research focused on the health effects of tobacco.

We suggest that rather than sponsoring a genuine "program of research into questions of tobacco use and health"[6] the CTR is a public relations vehicle intended to foster a false impression that cigarette manufacturers are interested in investigating the smoking and health "question." We believe such misuse of science raises serious ethical questions for scientists who accept funding through CTR or similar industry-supported entities. Even assuming that adequate funding is not available elsewhere, tobacco industry-supported scientists must ask themselves whether the value of their research in expanding the body of biomedical knowledge outweighs its utility in furthering the corporate interests of a business which kills 434,000 Americans every year.[9] □

TABLE 1—Beliefs About the Scientific Evidence Suggesting a Causal Relationship Between Cigarette Smoking and Various Illness Conditions

Illness/Condition	Strength of Causal Relationship with Cigarette Smoking: Strong %	Moderate %	Slight %	Not Established %
Emphysema	86.9	9.7	-	1.4
Chronic bronchitis	77.1	20.0	1.4	1.4
Heart disease	67.1	27.4	2.7	2.7
Low birth weight	51.8	30.8	12.9	4.8
Lung cancer	93.2	5.4	1.4	—
Cancer of the mouth, throat	76.1	19.4	1.5	3.0
Bladder cancer	24.8	56.3	15.8	28.1
Shorter life expectancy	76.4	16.7	4.2	2.8

TABLE 2—Beliefs About the Dangers of Environmental Tobacco Smoke, Smoking as a Primary Cause of Lung Cancer, and Smoking as an Addiction

Statement	Agree Strongly %	Agree Somewhat %	Disagree Somewhat %	Disagree Strongly %
The smoke from someone else's cigarette is harmful to a nonsmoker	52.9	41.4	5.7	—
Most deaths from lung cancer are caused by cigarette smoking	66.2	25.4	8.5	—
Cigarette smoking is addictive	83.3	15.3	1.4	—

TABLE 3—Mean Rankings of the Importance of 10 Areas of Research on Tobacco

Research Area	Mean Rank*	Standard Deviation	Percent Ranking Area as Top Priority
Tobacco use prevention	5.4	2.9	19%
Smoking cessation methods	5.2	2.8	14%
Neoplastic diseases	5.1	3.1	21%
Cardiovascular diseases	5.1	2.4	8%
Pregnancy and infant health	4.9	2.3	7%
Nonneoplastic respiratory diseases	4.8	2.3	—
Passive smoking	4.5	2.7	9%
Chemistry, pharmacology, toxicology	3.5	2.8	8%
Tobacco economics and legislation	3.4	3.4	12%
Tobacco advertising	3.4	2.9	4%

*Ranks range from low = 1 to high = 10.

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Gun-Related Deaths Increase Further for Black and White Young Men

The Department of Health and Human Services (HHS) reported today that one out of five deaths of teens and young adults in 1988 was gun related. Among young Black males, close to half of all deaths were firearm related.

Researchers at HHS' National Center for Health Statistics said the firearm-related death rate among Black and White males aged 15 to 24 years had declined in the early 1980s, but then rapidly increased from 1984 to 1988, especially for teenagers and particularly among Black males. Between 1984 and 1988, the firearm death rate among teenagers increased by over 40%, rising 20% from 1987 to 1988 alone, and reaching its highest level to date, 17.7 deaths per 100,000.

"This study shows that for the first time, the firearm death rates for both White and Black male teenagers exceeded the mortality from all natural causes of death," said HHS Secretary Louis W. Sullivan, MD. "For young Black males in particular, the excessive firearm and homicide death rates are appalling and heart-rending.

For Black males aged 15 to 19 years, the firearm death rate and firearm homicide rate more than doubled from 1984 to 1988, with an increase of 38% from 1987 to 1988 alone. By contrast, the nonfirearm homicide rate remained relatively stable. Black male teenagers were almost three times as likely to die from gun-related deaths than from all natural causes of death. For White males 15 to 19 years, the firearm death rate in 1988 for the first time exceeded that of natural causes, by 11%.

HHS Assistant Secretary for Health James O. Mason, MD, who heads the US Public Health Service, said, "The statistics show an American epidemic—without parallel in any other industrialized nation of the world. Physicians and other citizens need to work together to devise the same kinds of educational and prevention techniques that we use to attack other epidemics."

The findings are contained in a study, "Firearm Mortality Among Children, Youth and Young Adults, 1979–1988," produced by NCHS, a part of the Centers for Disease Control. The study examines homicide, suicide, and unintentional firearm deaths among those aged 1 to 34 years.

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Sandiford and Colleagues Respond

It is understandable that Richard Garfield is skeptical of our suggestion that improved access to health care was the factor most likely to have brought about the sharp fall in child mortality that began in Nicaragua in the mid-1970s. It has proven remarkably difficult to demonstrate such an impact in most parts of the world[1] (although Costa Rica may be an exception[2]), and despite massive assistance from the United States Agency for International Development, it is generally felt that one of the reasons for the downfall of Somoza's regime was its lack of investment in social programs. Indeed, these were our own prejudices at the time that we embarked upon this work. In fact, it was only after carefully eliminating alternative hypotheses (including most of those put forward by Garfield) that we finally accepted the concept that improvements in child health, at least in recent decades, are not inevitably the outcome of interventions or developments external to the health sector.

Of course, Garfield's problem, like ours initially, is to find a more plausible explanation for Nicaragua's breakthrough in child mortality. He starts by suggesting that it may be a delayed effect of economic growth in the 1960s. The trouble with such explanations is that, unless there is a lag period that can be justified a priori, it is not possible to explain any change on this basis. Nicaragua's last period of rapid economic growth ended in 1965.[3] While it is true that the impact of income growth on health status may be delayed, it is difficult to see how the boom of the early 1960s was still improving infant mortality 13 or 14 years later. The same is true of transport, communications, electricity, and potable water supplies, whose growth and decline in supply closely matched that of the overall gross domestic product.[3] Nor does urbanization account for the phenomenon. As our original article showed, the fall in mortality was apparently as rapid in rural as in urban areas and commenced at approximately the same time.

In contrast to the supply of energy, water, transport, and communications, the supply of government social services rose steeply in the 1970s and 1980s. This is in accord with our impression that the resources available to primary health care were increasing. That this spending was not entirely soaked up by expansion of hospital-based care is clear from the simultaneous increase in the number of health centers and decrease in the number of hospital beds per capita.

Some of Garfield's data should be viewed with caution. Particularly suspect are the data for the number of medical visits per capita. Not only are the figures different from those that we obtained from original sources in Nicaragua, but they also imply that each doctor in Nicaragua was seeing only about six patients per day. It is difficult to see how the number of visits almost tripled between 1978 and 1980 while the number of doctors in the country fell by almost 10%. Because all of these data depended upon the aggregation of statistics between different institutions, there was obviously plenty of scope for omission and overlap. In fact, the number of patients seen by doctors is probably not the most valid indicator of health care delivery, because it neglects the work of nurses and auxiliary nurses who were staffing most of the ambulatory care units in the country.

Regarding Garfield's assertion that only a quarter of the population had access to health care by the end of the 1970s, it should be pointed out that a single estimate gives no indication of whether coverage was improving or not. Using Garfield's own figures, the number of births in health institutions (in our opinion one of the better indicators of health service coverage) grew by an average of 6.0% per year from 1974 to 1978 but "only" by 4.2% per year from 1980 to 1986.[4,5]

Given the limitations in the available information, any explanation for Nicaragua's interesting trend in child mortality must rely to some degree on speculation, based hopefully on sound theory. However, our study and Garfield's response to it do illustrate both the potential and the pitfalls of analyzing and interpreting routinely collected health information.

Peter Sandiford, MBChB, MSc, MMedSc
George Davey Smith, MB BCh, M.Ed, MSc
Edward Cook, MB ChB

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Intimidation of CTR-Funded Scientists Claimed

The July 1991 Journal carried a Policy Forum discussion by Warner[1] and a paper by Cummings et al.,[2] berating scientists whose work is supported by the Council for Tobacco Research (CTR) for unspecified ethical failures and claiming that the work of those scientists only serves to reinforce doubts in the public mind about the severity of hazards of smoking.

Like many others, my associates and I accept research grants from government, unions, and industry, including CTR. We reported results, with acknowledgments for special grants from CTR when appropriate,[3] in more than a dozen leading public health, statistics, epidemiology, and other journals well known for the thoroughness of their reviews, including the *American Journal of Public Health*. Obviously, we had something to say that the reviewers and editors of these journals found worthy of publication despite scarce journal space and despite acknowledgment to the source of funds.

Any survey like those conducted by Warner and Cummings et al. into the beliefs of special groups of scientists raises the specter of censorship through intimidation. To suppress scientific work because of its consequences is just another excuse for imposing censorship. Moreover, should one really discourage reviews of past research and the implementation of new smoking-related research that is critically oriented? Critical reviews of incorrect and misleading practices in smoking-and-health research serve to highlight erroneous methods and have an important hygienic effect on the conduct of science. At the same time they do not negate results of properly conducted investigations. But, more important, scientists must be free to pursue whatever appears promising to them. For instance, recent observations have shown that smoking is negatively associated with the relative risk of a number of very prevalent and important diseases and with the severity of their symptoms, primarily Alzheimer's, Parkinson's, and preeclampsia. Should such relevant research be suppressed because it might increase the sale of cigarettes? (Do scientific disagreements really affect the sale of cigarettes?)

It is unfortunate that individuals who are strongly dedicated to advancing a social good often appoint themselves as guardians of public morality.

I shall seek to publish a full reply to Warner and Cummings et al. in another journal. In the meantime I would be pleased to send a copy of that reply or reprints of our work to interested readers. (Telephone: (604) 733-1348/(604) 681-2701; fax (604) 681-2702). □

Theodor D. Sterling, PhD

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2. Cummings KM, Sciandra R, Gingrass A, Davis R. What scientists funded by the tobacco industry believe about the hazards of cigarette smoking. *Am J Public Health*. 1991;81:894–896.

Cummings et al. Respond

Dr. Sterling is incorrect in characterizing our article as an attempt to discredit and intimidate scientists funded by the Council for Tobacco Research (CTR). We do not question the motives of these scientists but rather the tobacco industry's motivation in continuing to support the CTR. Simply stated, we believe the goal of tobacco industry management is not to uncover the truth about smoking and health—it is to sell cigarettes.

We asserted in our article that the tobacco industry's purpose in funding the CTR is to manipulate and control the flow to the public of scientific information about smoking and health. A recent ruling from a tobacco liability case in New Jersey (Haines vs Liggett group) supports this assertion.[2] The judge, in ruling about the admissibility of documents in the case, concluded that the documents contained "explicit admissions" that the tobacco industry had used the CTR to support its legal defense needs.

Even today, the tobacco industry continues to deny the causal link between cigarette smoking and lung cancer. In response to a letter writing campaign by a fifth-grade class in Amherst, New York, an R.J. Reynolds spokesman wrote, "the simple and unfortunate fact is that scientists do not know the cause or causes of the chronic diseases reported to be associated with smoking. More scientific research is needed." The letter goes on to cite the industry's support of the CTR.

Our article demonstrates that almost all scientists funded by the CTR believe smoking causes disease and would disagree with the assertion in the R.J. Reynolds letter. The fact that a few scientists, such as Dr. Sterling, hold contrary views does not mean that there is significant controversy about tobacco and disease, as the industry wants people to believe, only that there is not unanimity. Neither public health policy nor personal decisions about health need await universal agreement that a substance is dangerous.

We had hoped our article would stimulate debate among scientists about the ethical dilemma of accepting funding from the CTR or similar industry-supported entities in light of the industry's possible uses of such participation. Apparently, we have succeeded. □

K. Michael Cummings, PhD, MPH
Russell Sciandra
Ronald M. Davis, MD

K. Michael Cummings, PhD, MPH, is with Roswell Park Cancer Institute, Buffalo, NY, Russell Sciandra is with the Tobacco Control Program of the New York State Health Department, and Ronald M. Davis, MD, is with the Michigan Department of Public Health, Lansing, Mich.

Requests for reprints should be sent to K. Michael Cummings, PhD, MPH, Smoking Control Program, Roswell Park Cancer Institute, Elm and Carlton Sts, Buffalo, NY 14263-0001.

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2. Lew JB. "Fraud!" Judge releases secret tobacco industry documents. *Tobacco on Trial*. February 28, 1992:1–5.

Warner Responds

Obviously, the articles by myself and Cummings et al.[2] have struck a raw nerve. Unfortunately, it was the wrong nerve, at least as relates to my article. (I would not presume to speak for Dr. Cummings and his colleagues.) The point of my Policy Forum article was to raise consciousness about the tobacco industry's use of its research-funding program as a public relations device, not to challenge the credibility of the research. Indeed, as noted in my article, little of that research actually relates directly to the dangers of smoking, and that which does typically supports the conventional wisdom on the subject. When the latter is pointed out to the industry, it is the industry itself that challenges the credibility of the science it has funded, invariably insisting that this work is inadequate, that "more research" is needed.

I concur with Dr. Sterling's conclusion that my article relates to "the specter of censorship through intimidation." Yet it is not my poll of the CTR Scientific Advisory Board that achieves this heinous outcome; rather, the documented experience demonstrates the industry's ability to intimidate its scientific consultants. The tobacco industry employs its economic muscle to intimidate a wide variety of individuals and institutions throughout our society, including legislators, the media,[3] and, apparently, elements of the scientific establishment as well.

If Dr. Sterling will take the time to reread my article, he will find only a single call to action. That is the seemingly modest suggestion that the CTR Scientific Advisory Board (SAB) issue a collective statement similar to that of their Australian counterpart, who wrote that "smoking is an important causative factor in several major diseases."[4] All of America's major health and medical organizations have taken this stand publicly. What stops the SAB? If it is truly independent (and free of intimidation), this would constitute a natural means of dissociating the science it purportedly represents from the distortionary use of the CTR program by the

August 18, 1965

MEMORANDUM

TI[illegible]0039002

FROM: Simon O'Shea

TO: W. T. Zoyt

SUBJECT: Planning

The Council has, during the last two years, passed through a period which was dominated by the events surrounding the preparation and issuance of the Surgeon General's Report and subsequently by congressional consideration of cigarette labeling legislation. During this period the general tone of The Council's public information activities has changed considerably and much staff activity has been devoted to assisting with the problems posed by the Surgeon General's Committee and the legislative deliberations.

The period of primary focus on governmental and legislative concerns may now be ending. However, the provision of the labeling bill which will require annual reports by various governmental agencies to the Congress undoubtedly will affect Council policy in the future. We should, at the earliest possible moment, try to learn whether these periodic reports will have the effect of continuing to mute industry's statements in the scientific field. It certainly must be considered that an open program of scientific discussion might draw governmental attacks on The Council.

In any case now is an obvious time to re-evaluate The Council's information program. It is neither possible nor intelligent to separate a review of Council information policies from its primary function in the field of scientific research. A good point at which to start a review is to consider what is the value of The Council to its industry sponsors. Some, but not all of these assets are:

(1) The existence of The Council demonstrates that the industry is acting in good faith in supporting a serious scientific effort to determine the effects of smoking on human health. Of course, the AMA program fills the same function.

(2) The Council provides the industry with a direct avenue of contact and intelligence in the field of medical research into tobacco use and health.

(3) The Council provides the industry with its own scientific experts who may also serve as scientific spokesmen.

(4) Research supported by The Council may either disprove the allegations that smoking is a primary etiological factor in some diseases or it may suggest ways of adapting or modifying cigarettes.

In the past, the Tobacco Industry Research Committee was active in the public discussion of whether smoking was related to certain diseases. Spokesmen of the Committee, over a period of a number of years, commented on virtually any report which was unfavorable to cigarette smoking. It seems unlikely that The Council will return to this type of public information activity and, indeed, a proposal for a return to such activity would probably adversely affect confidence in The Council, both on the part of the medical and scientific community and on the part of The Council's industry sponsors. In addition, the very volume of communications on smoking and health would now seem to preclude any attempt to counteract any but the most important statements in this field.

When the industry sponsors review the progress of The Council this fall they will, undoubtedly, begin their review by looking at the scientific program which is, after all, the primary reason for The Council's existence.

In order to be prepared for such a review, The Council should take its own scientific inventory. To my mind, The Council's reviews of its research program have not been sufficiently intensive. There is a tendency to add on projects without attempting to set down a full analysis of the state of knowledge in a particular field. I am sure that The Council's staff members have a general idea of the state of knowledge in a particular field but I do not believe we actually have it down on paper. Therefore, my first proposal is for a series of Research Reviews.

One of these Research Reviews should, at least, be prepared on each of the following topics: lung cancer, cardiovascular disease, respiratory diseases, chronic disease, epidemiology and, perhaps, bladder cancer.

Undoubtedly, there are other topics that should be the subject of formal review and it may be necessary to subdivide the topics listed above.

Each Research Review should encompass the following elements:

(1) A full analysis should be made of the state of knowledge existing regarding each disease or scientific topic, revealing or stating both what is known and what is unknown.

(2) Projects sponsored by The Council in the area of the particular topic of Review should be described and analyzed, in terms of their accomplished contribution or intended contribution to the state of knowledge regarding the subject under review.

(3) Each Research Review should list the gaps in knowledge and outline specific areas of future research as well as purpose of such research.

You will recall that my proposal for the 1964-65 Annual Report was very much like this idea for Research Reviews. The objection at that time was that it was beyond the resources of our staff. This is probably still true. However, it should be possible to commission such reviews by medical or scientific consultants. But, the Research Review on lung cancer should obviously have the very highest priority. The Associate Scientific Director could be freed of other duties in order to prepare the first such review which would serve as a model for other reviews prepared by commissioned consultants. I certainly am not just proposing more paper work. I believe, when completed, these research reviews will have multiple uses. These uses include the following:

(1) They will inform our industry sponsors of the state of scientific knowledge in those research fields which are of greatest interest to them, will describe the content of medical research sponsored by The Council and its relation to research going on in the general scientific community, and they will finally outline concrete future scientific research proposals as well as the objectives of such proposals.

(2) These Research Reviews can be presented to, and discussed with the SAB in an effort to create a more concrete frame of reference for the actions of the Board.

(3) These Research Reviews, when prepared by the commissioned consultants, would obviously be of value to the scientific community (specific reference to The Council can be eliminated or modified). If we are satisfied with a Review we could encourage its publication.

(4) These documents would be of great value in dealing with the lay press. They would be an ideal background resource when questions arose concerning a specific scientific problem. Upon publication of a Research Review in a scientific journal it could be promoted with science writers.

(5) Such concrete analytical reviews would certainly be suitable for distribution to practicing physicians and would have a specificity and concreteness that we seem to feel our Annual Report lacks.

Our experience with Sterling might seem to suggest some pitfalls that would affect this proposal. However, it should be remembered that Sterling was commissioned to work in the specific context of the Surgeon General's Report while commissioned consultants in this case would try to summarize current scientific knowledge without any special polemic intent. Furthermore, it seems to me that we could work out our own formula for these Research Reviews if we did prepare the first one on lung cancer within our own staff. However, even in this case it might be good to get some outside thinking. Perhaps Rhoyer in retirement will also review this topic for us. This proposal certainly requires a great deal of effort and time and, in some cases, even money, but it seems to me the only practical way to get a coherent overall view of the research situation. It doesn't seem likely that the AMA or the federal government is going to do this job for us and perhaps indeed that is one of the attractions of the proposal. Without

this kind of analysis it is very difficult to establish research priorities or interest the BAB in the concept of research priorities. We won't have to start from scratch. Our own submissions to the Surgeon General are a resource as all the research papers in the report of the President's Commission on Heart Disease, Cancer and Stroke.

The foregoing proposal serves a number of public relations as well as scientific purposes. In effect it recognizes that The Council is primarily a scientific organization and attempts to advance this scientific program. In considering information activities that might be undertaken by The Council, two basic goals present themselves.

(1) The public information activities should seek to tell the story of what The Council is and what it does. Such public information activity demonstrates the good will and the public concern of the sponsors of The Council. It also demonstrates by the very breadth of research currently going forward that questions regarding tobacco use and health are far from being resolved.

(2) The Council out of its own knowledge of the general research situation and out of knowledge of Council sponsored projects is in a position to comment publicly on theories regarding the effects of tobacco use on human health and disease. In no special order, here are some public information activity proposals.

A. INTRA-INDUSTRY ACTIVITIES

The Council has a continuing need to keep its sponsors informed of the purpose and accomplishments of its program. During the past two years this kind of activity has been much reduced. The Council should once more seek opportunities to appear before various industry groups and associations in order to explain its program, and these speaking appearances should be supported by appropriate local publicity efforts. The Council can serve a real purpose in keeping up the morale of industry workers at all levels in regard to the scientific questions concerning cigarette smoking. Speeches or talks before industry groups should be as simple and non-technical as possible. A conviction that The Council serves a real purpose at the level of growers, warehousemen, wholesalers and retailers would certainly be appreciated by the manufacturing sponsors. Efforts should be made to obtain a better understanding of the program on the part of the manufacturing sponsors themselves. Certainly one of the avenues toward this end would be the improvement of contact with industry research directors and staff. For this reason plans for some type of contact between industry research people and the BAB should be pushed forward as quickly as possible. Furthermore, the recent inclusion of industry research personnel in the informal conference on smoke exposure seems to provide a good precedent for future participation by industry people in such conferences.

3. OVERALL PROGRAM PUBLICITY

The possibilities for publicity on the overall program of The Council: what it does, how it operates, what it has learned are by no means exhausted. The Today's Health story on the AMA tobacco health program is a good example of this type of publicity. I think an attempt should be made through a personal contact to interest various publications in writing such stories. I would suggest these efforts first be made with friendly publications such as the Richmond, Charlotte and Louisville newspapers and in a few general medical publications such as Dr. Fishbein's "Medical World News." In each case, I would propose to get in touch with the editorial management of the newspaper or periodical and propose the preparation of an overall story on the research program of The Council.

In order to do this, I think we should be prepared either to have members of our scientific staff visit the publication involved or to underwrite the cost of staff writers visiting us here. We also should be prepared to put the individual staff writer in touch with Council grantees working in his own area. (For example, with Larson and Haff's team in Richmond.)

After setting up such stories a number of times we should gradually develop some expertise and then be in a position to approach some of the national publications such as the Wall Street Journal, National Observer and news magazines. The Today's Health article currently in preparation or one of the articles developing out of the work proposed above may very well or result in a good lay language description of our program which we might in turn reprint and use in place of our Annual Report as a general descriptive piece for use with the public.

In addition, to emphasizing our overall program, The Council should also devote some attention to developing stories on the work of individual grantees. Virtually, every scientific research organization does some public information work drawing attention to its sponsored research projects. This work would certainly have to be carried out with tact, but it is not excluded from the realm of possibility by any objections I have heard. As a first step I think it would be a good idea for me to make site visits with a member of the scientific staff to grantees and projects that we and they believe might be of interest to the press. These visits would give us a chance to evaluate the appeal of the project and the feelings of the grantee about obtaining publicity regarding his work. At the same time the contact would be made with the public information officer of the individual grantee institution in order to discuss their attitude towards publicity.

After these preparations, it should be possible to develop a story either in cooperation with the grantees institution or by direct approach to newspapers in the grantee's area. Merely putting these publicity recommendations into action would require considerable time and effort and that there is very little limit to how far the promotion of such stories might be carried.

Furthermore, it seems to me that The Council can continue and expand its effort to help individual grantees obtain publicity on their own publications. However, under their own letterhead rather than under the name of The Council. It seems to me that we might even volunteer the availability of this assistance to friendly grantees.

C. SPEAKING OUT ON SCIENTIFIC MATTERS

The ultimate publication of the Research Reviews proposed above would be one method for The Council to resume a discussion of the scientific situation regarding tobacco use and health. In addition, The Council should once more seek to arrange a limited number of speaking appearances by the scientific staff before medical and scientific groups. Such appearances seem to me legitimate public information activity of The Council. The resulting speeches should be publicized both at the local level and prepared far enough in advance so that they can be distributed to science writers and other members of the general press.

It has struck me that a very great deal is lost that might be drawn from our informal scientific conferences. We have already experienced the fact that it is possible to invite industry research people to these conferences. It seems to me that some type of written summary should be prepared on each of these conferences. I am told that at least once a press release was issued on one of the informal conferences. It seems to me that these conferences could still be kept off-the-record and yield some public information value.

Normally Dr. Hockett has close relations with at least one or two of the participants in these conferences. I would like to see Dr. Hockett and one or two such participants make themselves available at the conclusion of a conference to provide an informal press briefing on the particular subject to a group of New York science writers. Such a briefing need not in any way violate the off-the-record status of the conference and would give us personal contact with science writers and should not present too much of a problem of negative publicity since the subject of most conferences are technical, complex and still very much in the area of "not knowing." Consider the application of this proposal to the Oral Cavity Conference, for example.

D. THE SCIENTIFIC EXHIBIT

Our current exhibit is perfectly adequate for meetings of scientific organizations. We should view it as fundamentally telling the story of our research program and seek to have it scheduled where actual research workers will see it.

In addition, we should develop a separate exhibit which would be primarily addressed to general practitioners. The question then arises as to what we want to tell general practitioners and we will have to work this out. When this new exhibit is completed we should undertake to schedule it at state medical association meetings, particularly in areas whether we have not thus far appeared.

TO SUMMARIZE:

Our first priority should be to review the research program subject-area by subject-area. This will give us our own bearings, provide a basis of discussion with our sponsors, provide some rough guidelines for the SAB as well as give us a clearer story to tell the public. Outside consultants may bring some perspective to these reviews that we lack.

Activities to publicize the overall program of the Council have been outlined and efforts to publicize individual research projects recommended.

More emphasis on intra-industry communication is also proposed.

May .. 1971

MEMORANDUM

TO: Horace R. Kornegay

FROM: Fred Panzer

SUBJECT: The Roper Proposal

GENERAL COMMENTS

It is my strong belief that we now have an opportunity to take the initiative in the cigarette controversy, and start to turn it around.

For nearly twenty years, this industry has employed a single strategy to defend itself on three major fronts -- litigation, politics, and public opinion.

While the strategy was brilliantly conceived and executed over the years helping us win important battles, it is only fair to say that it is not - nor was it intended to be - a vehicle for victory. On the contrary, it has always been a holding strategy, consisting of

-- creating doubt about the health charge without actually denying it

-- advocating the public's right to smoke, without actually urging them to take up the practice

-- encouraging objective scientific research as the only way to resolve the question of health hazard

On the litigation front for which the strategy was designed it has been successful. While we have not lost a liability case, this is not because juries have rejected the anti-smoking arguments.

On the political front, the strategy has helped make possible an orderly retreat. But it is fair to say that it

has not stemmed the pressure for new legislation, despite the major concessions we have made.

On the public opinion front, however, our situation has deteriorated and will continue to worsen. This erosion will have an adverse effect on the other fronts, because here is where the beliefs, attitudes and actions of judges, juries, elected officials and government employees are formed.

THE STRATEGIC IMPASSE

As an industry, therefore, we are committed to an ill-defined middle ground which is articulated by variations on the theme that, "the case is not proved." As the recent history of U.S. involvement in Vietnam demonstrated, it is impossible to hold the public on a middle course for any length of time. There seems to be no way that mass public opinion can engage in a controversy and choose an answer that goes beyond the range of either/or.

In the cigarette controversy, the public -- especially those who are present and potential supporters (e.g. tobacco state congressmen and heavy smokers) -- must perceive, understand, and believe in evidence to sustain their opinions that smoking may not be the causal factor.

As things stand, we supply them with too little in the way of ready-made credible alternatives.

THE ALTERNATIVES

Two such credible alternatives exist:

1) The Constitutional Hypothesis
   i.e. people who smoke tend to differ importantly from people who do not, in their heredity, in constitutional makeup, in patterns of life, and in the pressure under which they live.

2) The Multi-factorial Hypothesis
   i.e. as science advances, more and more factors come under suspicion as contributing to the illnesses for which smoking is blamed -- air pollution, viruses,

food additives occupational
hazards and stresses.

Our 1970 public opinion survey showed that a majority (52%) believed that cigarettes are only one of the many causes of smokers having more illnesses. It also showed that half of the people who believed that smokers have more illness than non-smokers accepted the constitutional hypothesis as the explanation.

Thus, there are millions of people who would be receptive to a new message, stating:

> Cigarette smoking may not be the health hazard that the anti-smoking people say it is because other alternatives are at least as probable

The Roper Proposal would be a persuasive (if not strictly scientific) medium for this message , which we have done little to develop in a systematic or comprehensive way.

Following is my outline of the steps required to start a shift in public opinion if the Roper Proposal is accepted.

A SCENARIO FOR ACTION

1) Select a panel of experts to consult on the design of the study. Ideally they would be prestige figures who would initially have a solid contribution to make and who would also be willing to endorse the study publicly at a later stage.

2) Conduct the pilot study.

3) If favorable, present the results to carefully selected members of the following key groups:

Senate
House
Cabinet
White House
State Governors
Medical School and University Presidents
Scientific bodies

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The purpose is two-fold (a) to gain the support and participation of friends and (b) to neutralize any adverse action they may be brewing. For example: By seeing Secretary Butz at this time we might gain some degree of participation from the Agriculture Department. By seeing Secretary Richardson we might possibly forestall a PHS anti-smoking drive.

4) Conduct the full scale survey.

5) If the results are favorable, release them as a book in both hard cover and paper back version, hopefully published by a legitimate house. In effect, such a volume would be a counter - Surgeon General's Report. The principal authors would be Burns Roper and an eminent research scientist. The advisory panel-- hopefully broadened as a result of Step 3 -- would write the introduction. The industry's funding role would be fully acknowledged.

6) As a book the material would be marketed and promoted in all the many ways available: magazine condensation, TV and Radio talk shows, newspaper reviews and interviews, advertising, gift distribution, etc. etc.

And best of all, it would only have to be seen -- not read -- to be believed...just like the Surgeon General's report.

FP/kc

cc: M. Kastenbaum
W. Kloepfer, Jr.

1157

EXHIBIT 3

TOBACCO INDUSTRY RESEARCH COMMITTEE,
New York, N. Y., August 1, 1957.

Hon. JOHN A. BLATNIK,
Chairman, Subcommittee on Local and Monetary Affairs,
House Committee on Government Operations,
Washington, D. C.

DEAR MR. CHAIRMAN: When Dr. Little appeared before your subcomimttee on Thursday, July 18, 1957, he agreed to provide the committee with certain pertinent information concerning the research program of the Tobacco Industry Research Committee. Dr. Little has asked me to forward you this material. You will find it enclosed.

The Tobacco Industry Research Committee has appropriated for research grants $500,000 in each of the following years: 1954, 1955, 1956, and 1957. In 1956, a supplementary $200,000 was made available at the request of the scientific advisory board. Thus, the total available funds thus far amount to $2,200,000.

These funds have not been allocated exactly as appropriated, that is, on an annual basis. To date the total grant awards made by the scientific advisory board to independent scientists in accredited institutions amount to $1,832,591.51.

The addltional material, which Dr. Little agreed to supply the committee and which is appended, is:

1. A statement concerning the origin and purpose of the committee, issued at its inception.
2. A statement of policy adopted in 1954 concerning conditions and terms under which the scientific advisory board awards grants-in-aid.
3. A statement of the research program as adopted by the scientific advisory board in 1954.
4. An interim informal report of progress issued by Dr. Little, May 16, 1955.
5. The first formal report of the scientific director issued midyear 1956.
6. A list of the original grants showing the recipient of each grant, his institution, the value of the grant, and the date the project was initiated. Also, a similar list of renewed grants. This information is current as of July 1.
7. Thirteen abstracts of papers published in accepted scientific journals reporting on research work supported in whole or in part by grants approved by the scientific advisory board. These abstracts are for inclusion in the 1954 report of the scientific director, as yet unpublished, and have been approved by the investigator working on each grant.

Dr. Little has asked me to thank you for your courtesy in providing him the opportunity to appear before your subcommittee.

If you desire any further information, please let us know.

Sincerely,

W. T. HOYT, *Executive Secretary.*

ATTACHMENT A

STATEMENT CONCERNING THE ORIGIN AND PURPOSE OF THE TOBACCO INDUSTRY RESEARCH COMMITTEE AND ITS PROPOSED FUNCTIONS

The responsible chief officers of 9 of the cigarette and tobacco products manufacturing companies in America, and 5 organizations of growers of leaf tobacco and tobacco warehouse associations have formed the Tobacco Industry Research Committee in the interest of the public as well as of the industry to meet the challenge raised by widely publicized reports in the press, purporting to link tobacco smoking with the cause of lung cancer.

To avoid possible confusion and misunderstanding concerning the origin, purpose, and function of this committee, the committee makes the following statement:

I. EVENTS JUSTIFYING FORMATION OF COMMITTEE

The formation of the committee was prompted by the appearance of certain publications claiming an established relationship between cigarette smoking and lung cancer.

Typical of these reports is an article appearing in the Journal of the American Medical Association (143 JAMA 329, May 27, 1950) wherein Drs. E. L. Wynder and E. A Graham reported that applications of cigarette tars to the backs of mice had produced skin cancers.

In an address before the annual fall clinical conference of the Kansas City Southwest Clinical Society, held in Kansas City, Mo., on September 28, 1953, Dr. Alton Ochsner said: "This unprecedented increase in the incidence of bronchogenic cancer, we are convinced, is due to the carcinogenic effect of cigarette smoking" (Kansas City Medical Journal, vol. XXIX, No. 6, November-December, 1953, at p. 6).

At a recent meeting of the Greater New York Dental Association, these same doctors reiterated charges, based on statistical and other analyses, that cigarettes contain a cancer-producing factor. These assertions, and others to the same effect, have been given extensive publicity in magazines of national circulation, such as Time (November 30, 1953), Life (December 21, 1953), and Reader's Digest (December 1953), and in countless national, regional, and local newspapers.

Examination of all recent reports and publications, however, reveals that many factors, such as various types of air pollution as well as tobacco smoke, have been suspected as causes of lung cancer. Although much has been written concerning the incidence of lung cancer, there is still a dearth of authoritative findings on the subject. It is safe to say that no persuasive and definitive conclusion respecting the cause of this disease, or the relation of smoking thereto, has been established.

In the light of the foregoing agitation and in the absence of authoritative findings, there is a responsibility on the part of the management of the tobacco manufacturers and others engaged in the tobacco industry to aid in the final determination of this controversy. It is the earnest wish of the industry to encourage competent scientific authority to find ultimate facts which will dispel the present confusion and to communicate authoritative factual information on the subject to the public.

II. PLAN OF ACTION

The committee announced in a full page advertisement appearing in 448 newspapers circulated throughout the United States on Monday, January 4, 1954, that it would meet the challenge of these reports. The signing members of the Tobacco Industry Research Committee pledged to support by financial aid, in addition to that already contributed by individual companies, research under the charge and direction of a scientist of unimpeachable integrity and national repute. To guide and advise in this field, scientists disinterested in the cigarette industry and of recognized ability and professional standing in medicine, education, and associated sciences will be invited to act as an advisory board.

This statement was subscribed to by the following companies, which now make up the committee:

The American Tobacco Co., Inc., by Paul M. Hahn, president
Benson & Hedges, by Joseph F. Cullman, Jr., president
Bright Belt Warehouse Association, by F. S. Royster, president
Brown & Williamson Tobacco Corp., by Timothy V. Hartnett, president
Burley Auction Warehouse Association, by Albert Clay, president
Burley Tobacco Growers Cooperative Association, by John W. Jones, president
Larus & Bro. Co., Inc., by W. T. Reed, Jr., president
P. Lorillard & Co., by Herbert A. Kent, chairman
Maryland Tobacco Growers Association, by Samuel C. Linton, general manager
Philip Morris & Co., Ltd., Inc., by O. Parker McComas, president
R. J. Reynolds Tobacco Co., by E. A. Darr, president
Stephano Bros., Inc., by C. S. Stephano, Sc. D., director of research
Tobacco Associates, Inc., an organization of flue-cured tobacco growers, by J. B. Hutson, president
United States Tobacco Co., by J. W. Peterson, president

III. FORMATION OF THE COMMITTEE

Mr. Paul M. Hahn, president of the American Tobacco Co., on December 10 and 11, 1953, took the initial steps in the formation of the committee in a telegram sent to the following people:

Joseph F. Cullman, Jr., president, Benson & Hedges
E. A. Darr, president, R. J. Reynolds Tobacco Co.
B. F. Few, president, Liggett & Myers Tobacco Co.
William J. Halley, president, P. Lorillard Co.
Timothy V. Hartnett, president, Brown & Williamson Tobacco Co.

J. B. Hutson, president, Tobacco Associates, Inc.
O. Parker McComas, president, Philip Morris & Co., Ltd., Inc.
J. Whitney Peterson, president, United States Tobacco Co.

Mr. Hahn suggested that these heads of the leading tobacco units meet to consider some action in response to these published reports. Thereafter, those invited, with one exception,[1] met on December 14 and 15, 1953, and December 28, 1953, in New York City.

At these meetings the conclusion was reached that the tobacco industry must take public action to meet these widely publicized claims. The committee was formed, and the firm of Hill & Knowlton, Inc., of 350 Fifth Avenue, New York, N. Y., was engaged to assist the committee in effectuating its purpose.

The officers of the committee selected were Paul M. Hahn, chairman; J. Whitney Peterson, vice chairman; Joseph F. Cullman, Jr., treasurer; and Wilson T. Hoyt, of Hill & Knowlton, Inc., secretary. It was the expressed intention of the committee to have the chairmanship of the committee rotated every 3 months. It was agreed that expenses for the committee's activities, including expenditures for research, the advertising, the employment of Hill & Knowlton, and other similar expenses, would be defrayed by donations from the member firms based on their volume of business and by contributions to be agreed upon by other members. Arrangements were then perfected for insertion of the advertisement referred to in the newspapers throughout the country.

The Bright Belt Warehouse Association, the Burley Auction Warehouse Association, the Burley Tobacco Growers Cooperative Association, Larus & Bro. Co., Inc., the Maryland Tobacco Growers Association, and Stephano Bros., Inc., were invited to join with the original group and became members of the committee.

IV. LIMIT OF POWERS

The purposes and objectives of the committee are to aid and assist research into tobacco use and health, and particularly into the alleged relationship between the use of tobacco and lung cancer, and to make available to the public factual information on this subject. It is the considered judgment of the committee that its activities shall be confined to the purposes set forth above, and that it is in nowise to be considered or to operate as a trade association or to participate in any activity or give consideration to any matters affecting the business conduct or activities of its members, and that its activities in every respect shall conform to law and all decrees or judgments of courts affecting or relating to the tobacco industry. To this end the committee is proceeding under the advice of legal counsel selected from among the counsel or nominees of its members.

TOBACCO INDUSTRY RESEARCH COMMITTEE,
PAUL M. HAHN, *Chairman.*

NEW YORK, N. Y., *January 25, 1954.*

ATTACHMENT B

TOBACCO INDUSTRY RESEARCH COMMITTEE STATEMENT OF POLICY CONTAINING CONDITIONS AND TERMS UNDER WHICH PROJECT GRANTS ARE MADE

(Adopted by the Scientific Advisory Board)

1. General policy

The Tobacco Industry Research Committee is dedicated to the support of the investigation of fundamental matters relating to a connection between tobacco use and human health. In so doing the Tobacco Industry Research Committee recognizes the importance of independent research by competent investigators. Research policy and programming are the responsibility of the Scientific Advisory Board. Grants are made only after careful consideration by the Scientific Advisory Board of the merits of proposals and of the qualifications of the individual and his institution undertaking the work.

The Committee desires to have scientists work with the greatest freedom and without domination of any kind. It will make no attempt to direct the administration of the project once started, to influence its course or to control its results other than to be assured that the funds are properly expended for the purposes of the grant and that all findings are reported in accordance with the best scientific practice.

[1] Liggett & Myers Tobacco Co.

II. Payments and budgets

Unless otherwise requested at the time of initiating a specific grant, payments will be made quarterly in advance to the institution at which research is being conducted.

Grants may not be transferred from one institution to another due to a change in affiliation by the principal investigator without express permission.

The contract for a grant may be terminated prior to normal expiration date by the grantee upon notification to the Executive Secretary of the Tobacco Industry Research Committee with a statement of the reasons for termination.

Budgets are presumed to be accurate at the time of issuance of a grant. However, if for unforeseen reasons, additional funds or reapportion of funds are required such request will be considered upon receipt of a complete statement of reasons for such change.

At the time of expiration of a grant or in the event of its termination, unexpended funds shall be returned to the Tobacco Industry Research Committee. If, at such expiration or termination, additional projects are anticipated and are approved such funds may, upon request, be applied against the new grant at the time of its issuance.

III. Reports

Grantees are to furnish a report of activities semiannually. These need not be extensive but should be sufficiently informative to permit the Scientific Advisory Board of the Tobacco Industry Research Committee to know who is being accomplished. At the conclusion of a project a detailed report is expected which shall be given in writing to the Scientific Advisory Board.

An expenditure report should be made by the grantee semiannually.

IV. Exchange of information

With the consent of the grantee, the Scientific Advisory Board may recommend the exchange of interim information between investigators working on different projects if the interim results indicate a relationship between projects. This would only be done with the object of assisting and expediting work in process.

V. Publication and public information

The Tobacco Industry Research Committee approves the initial presentation by the investigator of research results only in accepted medical and scientific journals or before accepted medical or scientific societies. It has no objection to dissemination to the public of any or all final conclusions from projects in these ways.

Information from semiannual or final reports will be released publicly only with the permission of the investigator.

When a journal or society schedules the presentation of any findings from a project the Scientific Advisory Board will expect a statement or abstract from the grantee covering the date and general subject matter of his presentation.

While no special funds are provided to assist publication of results covering costs of illustrating, typesetting or other expenditures, the Tobacco Industry Research Committee will consider a request for such funds upon presentation of the manuscript to be published.

ATTACHMENT C

THE RESEARCH PROGRAM OF THE SCIENTIFIC ADVISORY BOARD TO THE TOBACCO INDUSTRY RESEARCH COMMITTEE

THE SCIENTIFIC ADVISORY BOARD

Members of the Scientific Advisory Board to the Tobacco Industry Research Committee are:

Chairman and Scientific Director: Clarence Cook Little, Sc. D., LL. D., Lit. D., Director, the Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine

McKeen Cattell, Ph. D., M. D., Professor and Head of the Department of Pharmacology, Cornell University Medical College, New York, N. Y.

Julius H. Comroe, Jr., M. D., Chairman and Professor, Department of Physiology and Pharmacology, Graduate School of Medicine, University of Pennsylvania, Philadelphia, Pa.

Leon O. Jacobson, M. D., Professor of Medicine, University of Chicago, Director, the Argonne Cancer Research Hospital, Chicago, Ill.
Paul Kotin, M. D., Assistant Professor of Pathology, University of Southern California Medical School, Los Angeles, Calif.
Kenneth Merrill Lynch, M. D., Sc. D., LL. D., President, Dean of Faculty, and Professor of Pathology, Medical College of South Carolina, Charleston, S. C.
Stanley P. Reimann, M. D., Sc. D., Scientific Director, the Institute for Cancer Research, Director, the Lankenau Hospital Research Institute, Philadelphia, Pa.
William F. Rienhoff, Jr., M. D., Associate Professor of Surgery, Johns Hopkins School of Medicine, Baltimore, Md.
Edwin B. Wilson, Ph. D., Professor Emeritus of Vital Statistics, Harvard University, Cambridge, Mass.
Associate Scientific Director: Robert C. Hockett, Ph. D.

THE RESEARCH PROGRAM

The Tobacco Industry Research Committee, formed in January 1954, to sponsor independent research into tobacco use and health, put into the hands of a Scientific Advisory Board the development and continuing supervision of a research policy and program. Many doctors, educators, and scientists want to know about the Committee, the Scientific Advisory Board, the purposes and policies, and the research program. This booklet is intended to answer these questions.

"The Committee's approach has given the Scientific Advisory Board an unusual, if not unique, opportunity to foster and guide the widest possible range of research by outstanding scientists and doctors under conditions of utmost freedom," according to Dr. Clarence Cook Little.

Board determines activities

Because of the broad responsibility of the Scientific Advisory Board, scientists whose competence is securely established in their respective fields of knowledge are asked to serve as its members. They are given assurance of complete scientific freedom in their work.

The Scientific Advisory Board does not contemplate conducting specific laboratory investigations as a Board. This does not rule out the possibility, however, that individual members may seek and, in competition with other applicants, obtain a research project under a Tobacco Industry Research Committee grant. This is the policy common to similar bodies such as the Committee on Growth and the National Advisory Cancer Council.

The Board members retain completely their association with their institutions and, except for the Scientific Director, are reimbursed only for time and expenses involved in their services to the research program.

The Board determines the scope and direction of the research program; reviews and solicits requests for research grants from universities, hospitals and other recognized research organizations or from individuals there situated. Regular monthly meetings are held by the Board to carry out its scheduled work. In addition, members of the Board frequently undertake special assignments in connection with the development of the research program.

Scope of interests defined

Before undertaking a large-scale program of recommending grants to finance research projects, the Scientific Advisory Board laid the foundations on which a series of research projects could be developed and coordinated. First was the delineation of the scope of interests within which investigations should be sponsored. Second was the organization of a program to assure that necessary investigation was undertaken without unnecessary duplication of work.

Scope covers three main areas

The outline of interest sets out three main areas of investigation:

1. The physical and chemical composition of tobacco and accompanying products, such as cigarette papers and additives. This covers the preparation, fractionation and analysis of tobacco and of added substances.

2. Tissue changes in humans as well as in animals, in normal life or under laboratory conditions, subjected to various types, duration, and intensity of exposure to various tobaccos and derivatives, and other potential irritants. Tissues of special interest are those of the mouth, lungs, glands, heart, and other organs of subjects of various ages, sex, and strains.

3. Smoking and other tobacco habits, and the emotional and physical makeup of smokers, with respect to establishment, duration, and intensity of tobacco use, and correlation of these data with metabolic, glandular, and nervous types under various degrees of stress and challenge.

It is recognized that work has been done and is being done here and abroad in these fields. The Scientific Advisory Board plans to avoid repeating work that has produced accepted results, as in the field of the constituents of tobacco. Where results have been inconclusive, however, considerable further careful study and well-planned research is indicated.

The program takes shape

In its second step, the Board developed a coordinated research program intended not only to ascertain facts with respect to the questions raised concerning tobacco use and health but also to contribute to further understanding of cancer, heart disease, and other public-health problems. The program is intended to produce clinical and experimental findings necessary before valid conclusions can be made regarding possible relationships between tobacco use and human health.

Among research projects being sponsored is the study of human lung cancer in several major medical centers in the United States. A uniform method of study will allow for a comparison of the frequency and types of lung cancer in the geographic areas investigated. Such related factors as length of residence, occupational history, personal habits and associated diseases will be reviewed for possible relation to the causes and onset of lung cancer. It is expected that this research will furnish clues for still further research to be supported by the Committee.

Research projects

Research projects, to be supported at sites to be selected, will be encouraged in the following general subjects (primary responsibility for overall advice and informal guidance has been assigned to individual Board members, as indicated in parentheses):

Inhalation of smoke.—Carefully planned and regulated experiments will be conducted with mammals subjected to inhalation of tobacco smoke under controlled conditions. (Dr. Kotin.)

Direct application of smoke tars.—Projects will test the effect of identified smoke tars, derived under controlled conditions, on tissues of animals with varying degrees of susceptibility to cancer or other ailments. (Dr. Reimann.)

Study of lung tissues.—Projects to study lung tissues in living animals and man will be undertaken. (Dr. Reinhoff, Dr. Lynch, and Dr. Reimann.)

Malignant changes in tissues.—Studies of malignant changes of tissues will be made under laboratory condition. (Dr. Jacobson.)

Study of cardiovascular tissues.—Studies will be made of changes involving degeneration or unbalance in cardiovascular tissues. (Dr. Comroe.)

Habits and characteristics of smokers.—A series of surveys of selected populations in various parts of the country will be undertaken concerning the characteristics of human smokers and nonsmokers, including age, sex, emotional habits, environmental factors, and exposure, as well as smoking habits. (Dr. Wilson.)

Preparation and analysis of tobacco derivatives.—Sources will be developed for a continuous supply of tars from tobacco smoke and its derivatives that can be used in various experiments. Efforts will be made to duplicate human smoking in machines. Production of the derivatives will be regulated so as to have full knowledge of the conditions under which smoking is simulated. (Dr. Cattell.)

Initial research grants under the approved program went to scientists at such institutions as the University of Southern California, the University of Texas, the Temple University School of Pharmacy, Mount Zion Hospital at San Francisco, the Medical College of Virginia, Fordham University, Harvard University, Roswell Park Memorial Institute at Buffalo, New York University-Bellevue Medical Center, Tufts College Medical School, University of Pennsylvania Department of Surgery, the Medical College of South Carolina, and the College of Physicians and Surgeons at Columbia University.

Many new research projects are being considered continually by the Scientific Advisory Board, and approval of grants are announced from time to time.

ADMINISTRATION OF GRANTS

The Scientific Advisory Board welcomes proposals from qualified research groups or organizations for specific research projects. The Board also is authorized to originate proposals which it believes will contribute to the program and to seek appropriate individuals and institutions to carry out such projects under a Tobacco Industry Research Committee grant.

Each applicant and prospective recipient of a grant receives a statement of policy approved by the Scientific Advisory Board.

The statement of policy declares that the Tobacco Industry Research Committee "desires to have scientists work with the greatest freedom and without domination of any kind. It will make no attempt to direct the administration of the project, once started, to influence its course or to control its results other than to be assured that the funds are properly expended for the purposes of the grant and that all findings are reported in accordance with the best scientific practice."

Forms of application

Standard application forms are sent to those desiring to apply for grants from the Tobacco Industry Research Committee. The applications are submitted to the Scientific Director and to each other member of the Scientific Advisory Board for study and comment. When indicated, personal communications or visits are made with the applicant in order to clarify or expand his proposal.

Each application is measured against such criteria as the following:

1. Is the proposal relevant to the scope of the program?
2. Is it made by a competent individual or institution?
3. Will it contribute to knowledge of the subject?
4. How does it rank in importance with other projects underway or under consideration?
5. Does it promise results not already contemplated from other research projects?
6. Can it be of value as a check against work already being carried on?

The Board discusses and reviews all applications in regular meetings and recommends grants for the approved applications. Grants are then made by the Tobacco Industry Research Committee.

Unless otherwise requested or agreed, payments are made quarterly in advance to the institution at which research is conducted. Grants may be transferred from one institution to another, where there is a change in the affiliation of the principal investigator, if permission is obtained.

Grantees are to furnish a report of activities semiannually. These should be sufficiently informative ot permit the Board to know what is being accomplished. A detailed report is expected by the Scientific Advisory Board at the conclusion of a project.

EXCHANGE OF INFORMATION AND PUBLICATION

With the consent of grantees, the Scientific Advisory Board may recommend the exchange of interim information between investigators working on different projects if interim results indicate a relationship between projects. The only purpose of this exchange of information is to assist and expedite work in progress.

The Tobacco Industry Research Committee approves the initial presentation of research results by the investigator only in accepted medical and scientific journals or before accepted medical or scientific societies. It has no objection to dissemination to the public in these ways of any or all final conclusions of the investigators.

When a journal or society schedules the presentation of any findings from a project, the Scientific Advisory Board expects the grantee to furnish a statement or an abstract covering the date and general subject matter of his presentation.

Information derived from semiannual or final reports will be made public by the Committee only with the permission of the investigator.

While no special funds are provided to assist publication of results covering costs of illustrating, typesetting, or other expenditures, the Tobacco Industry Research Committee will consider requests for such funds upon presentation of the manuscript to be published.

THE TOBACCO INDUSTRY RESEARCH COMMITTEE

The Tobacco Industry Research Committee was organized early in 1954 and is comprised of six tobacco manufacturing companies and eight associations of tobacco growers and warehousemen. Timothy V. Hartnett, former president of Brown & Williamson Tobacco Corp., is chairman.

The purposes and objectives of the Committee are to aid and assist research into tobacco use and health and to make available to the public factual information on this subject.

In the light of wide publicity given to some statistical studies attempting to link tobacco use and lung cancer, the Tobacco Industry Research Committee believes it has a public responsibility to aid in the further search for conclusive answers to cancer and other public health problems. It accepts a lasting interest in people's health as a basic premise in offering tobacco products for sale.

Examination of recent reports and publications and of standard literature on the disease indicate that many factors, such as various types of air pollution, are suspects in lung cancer and other ailments. Medical and research scientists agree that no persuasive, definitive, and final conclusion has been established with respect to the cause or causes of this disease.

The fact that cigarette smoking today should even be suspected as a cause of serious disease is a matter of deep concern to the tobacco industry. Accordingly, the Committee pledges aid and assistance to the research effort into all phases of tobacco use and health.

STATEMENT BY DR. LITTLE

"The Scientific Advisory Board of the Tobacco Industry Research Committee has certain opportunities and obligations of tremendous importance to the future development of scientific research in the United States.

"First, it can recommend financial support of basic or pioneer research on its own evaluation of individuals or institutions on the basis of promise or faith rather than on a purely factual and materialistic standard. Pioneer research is the creative 'idea' phase of discovery. It is the absolutely essential forerunner of progress to the 'project' stage!

"Second, the Board can itself plan and initiate research in fields and for purposes not now being covered. This is, I believe, an entirely new departure for any industry. Granting a group of scientists the power of creating new research activity is a great and exciting development.

"If we on the Board have the wisdom and vision to plan creatively, we may be able to justify this confidence placed in us. If we do justify it, the tobacco industry will have made its greatest contribution of service to mankind and may well establish a precedent and pattern which other industries will follow in support of research."

C. C. LITTLE.

ATTACHMENT D

A REPORT OF PROGRESS

Statement of Dr. Clarence Cook Little, Scientific Director, the Tobacco Industry Research Committee, and Chairman, the Scientific Advisory Board. Made at discussion with science writers, Monday, May 16, 1955, Tobacco Industry Research Committee offices, 5320 Empire State Building, New York, N. Y.

A year has gone by since the Scientific Advisory Board to the Tobacco Industry Research Committee first met to discuss the course of scientific research to be financed by grants from this industry group.

At that time, many of us were strangers personally, though not scientifically. As members of a newly created Scientific Advisory Board, however, we had at least three essential things in common.

First, we had been given a free rein to spend an industry's research fund as we thought best. That in itself was a challenge and responsibility.

Secondly, we shared a firm belief that sound scientific research would continue to unfold, however gradually, the solutions to perplexing health problems.

Thirdly, and importantly, we were in full agreement that the arena of public controversy was to be avoided in the interest of constructive science and genuine progress.

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