

Presentation to the Philip Morris Incorporated
Board of Directors, April 30, 1975

Gentlemen:

Slide 1
Tower

In 1973 when I was last privileged to appear before you, we were dedicating our new tower laboratory and expanded R&D facilities.

Slide 2
Dedication

You may recall that we were also hosting the First Philip Morris Science Symposium, an event which was to be recognized at home and abroad as a significant milestone in our progress towards establishing the premier tobacco product research establishment in the world.

Slide 3
Triangle

The goal of Research & Development is to anticipate every possible scientific and technical challenge to our business and to meet those challenges in the most effective manner. To do this we must achieve the orderly transition of scientific findings to technological developments and marketable products. We in Philip Morris U.S.A. feel we have achieved this successful reduction of R&D to practise. It has come about through the insistence of Clifford Goldsmith on open-communications between all departments. This approach underlies many of our new product and process developments. I am sure you are familiar with many of them so I will not take time to describe them again.

Instead, for this morning I have been asked to summarize for you recent technical developments as they relate to the industry problem

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of smoking and health. Because of the scope of this subject, I hope you will forgive me if I oversimplify in some places. In this review I will first chronicle developments leading to the situation as it exists today. I will then discuss activities currently underway in various laboratories throughout the world.

Although tobacco has been under attack from the beginning of its use in Western culture, the recent thrust against cigarets involved three major events:

Slide 4
Dahl & Hill

The first of these were the epidemiological studies published around 1950 which purported to show a strong statistical association between smoking and lung cancer.

Slide 5
Wynder Publ.

The second was the report by Wynder and coworkers in 1953 that chemicals in the so-called tar portion of the smoke produced skin cancer on selected strains of mice. This early slide illustrates his

Slide 6
Wynder
graph

results and show that the data fit a classical dose response pattern of biological activity, thereby adding weight to his conclusions. The result of this demonstration was the tar derby started by the publication

Slide 7
Reader's Dig.

of values for brands in the Reader's Digest.

Slide 8
Surg. Gen.
Report

Eventually all of this led to the report of the U.S. Public Health Surgeon General's Advisory Committee on Smoking and Health which recommended that action be taken to curb the alleged disease effects of

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smoking. As a result we now have anti-cigarette advertisements, warning label on the package, prohibition of electronic media advertising, testing and publication of tar and nicotine numbers by the Federal Trade Commission, cigarette tax differentials based on the delivery of tar, a Smoking and Health research program in the National Cancer Institute to find a so-called less hazardous cigarette, and most recently, a rash of local prohibitions on smoking in public places, presumably to protect the nonsmoker from the environmental smoke generated by nearby smokers. Other countries have followed the lead of the U.S.A. in taking actions such as these against the cigarette industry.

Most scientists agree that statistical association does not prove causation. In cigarette smoking and health, as in many other chronic diseases, several other conditions must be met to make a convincing case for a cause-and-effect relation. In the first place, there must be some relation between the risk of developing the disease and the quantitative exposure to cigarette smoke -- the dose-response relationship mentioned earlier. Secondly, there must be some plausible, verifiable mechanism explaining how the chemicals in the inhaled smoke give rise to the disease process. And thirdly, the disease must be reproducible in some bioassay system at least remotely resembling the human situation.

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Slide 10
Labs with
programs.

today
There are at least a dozen major biomedical research programs in the world dedicated to the objectives I have just outlined. Some are listed on this slide. The first ~~of these~~ was established about 1952 by Dr. Wynder at the Sloan-Kettering Institute for Cancer Research and was closed out after about 19 years of operation.

Slide 11
German
Res. Inst.

About 10 years later a second program was begun at the Research Institute of the German Cigarette Industry in Hamburg. Their scientists carried out massive scale mouse skin painting bioassay of various cigaret smoke condensates. They made the first major attempt to relate the chemistry of the smoke to the biological effects, and the first effort to relate the mouse skin painting results to smoke inhalation results in hamsters. They showed that various tobaccos had different effects in the mouse skin test. They identified some fractions of smoke condensate which were more potent in this respect than others. ~~And~~ *although* they have not been able to demonstrate lung cancer by inhalation, *even though* they claim to have developed precancerous lesions in the larynx of certain species of hamsters. *This claim is the subject of criticism by several pathologists who have examined the evidence.*

Slide 12
Harrogate

About the same time a major effort was also being made in Great Britain also under industry sponsorship. Initially the industry organized a jointly sponsored biological research program through the Tobacco Research Council with laboratories at Harrogate. They also

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set up massive skin painting experiments and demonstrated that various tobacco and tobacco fractions exhibited differing biological activities.

But As soon as this critical point in the program was reached, the British company sponsors abandoned this line of work, since they felt they had now reached the stage at which each company must make its own tobacco blends and carry out tests on its own product formulations.

Slide 13
NCI

Meanwhile we have had the development of a major program in *out USA*, the National Cancer Institute aimed at the development of a less active cigaret. This program, now about seven years old, is currently at a budgetary level of about eight million dollars per year. It is administered by NCI staff with an advisory group known as the Tobacco Working Group, a mixture of university, government, and industry scientists expert in various aspects of the problem. This program has generally confirmed the earlier results obtained in the Hamburg and other laboratories. It is now moving in the direction of "product development," that is, combinations of tobacco formulations, filters, paper, etc., which will give rise to smoke of lowered biological effects. It is also progressing in the direction of trying to confirm mouse skin painting results by inhalation tests with dogs in Auerbach's laboratory of the Veterans Administration and at Battelle Northwest Laboratories of the AEC. Rat inhalation tests are being developed at Oak Ridge National Laboratories in Tennessee. Two major

Slide 14
NCI Report

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publications summarizing early results of this program are due to appear this summer and fall.

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It is interesting at this point in our discussion to step back a bit and contemplate the underlying basis for all this frantic activity. Two decades ago when the public health authorities, regulatory agencies, anti-cigarette zealots, and certain self-righteous commercial interests, such as the Reader's Digest, loudly proclaimed the dangers of cigarette smoking, the solution at least to them seemed very simple -- STOP SMOKING. Well, as you know, after twenty years it hasn't happened. People who want to smoke keep right on doing it. So now the watchword is "to reduce the so-called hazards of smoking." This movement has involved numerous scientists and considerable commercial effort as we shall see in a moment. It has developed a strong momentum of its own which totally ignores the basic question of whether or not cigarettes are harmful to health.

The reduction of tar and nicotine delivery is one approach to the supposedly safer cigarette. It is based on the dose-response relationship which I have mentioned earlier. If the cigarette delivers less smoke, the smoker consuming the same number of cigarettes in the same manner as before receives less dose and presumably has a lowered risk of disease.

Slide 16
Reduced tar

As you well know, the tar deliveries of American cigarettes have been substantially reduced during the last twenty years. Dr. Wynder has

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often said the industry has already contributed greatly to reducing the health hazard by producing lower delivery cigarettes. In a recent publication he has even described confirming epidemiological data to support this statement.

Slide 17
Cigts. less
biol. act.

In theory, a second way to reduce the presumed hazard of smoking is to reduce the specific biological activity or toxicity of the smoke.

Conceivably this could be done by modifying the tobacco blend mixture, or by treating the tobacco some way, or by selective filtration of smoke components, or by substituting for the tobacco some other material which will produce a ^{supposedly} "less harmful" smoke. All of these possibilities are being investigated. And all of them are faced with an almost insurmountable problem from a technical point of view: / that is how to

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demonstrate that cigaret smoke is less harmful when we have no satisfactory way to demonstrate that it is harmful, particularly to humans.

(Incidentally, this is also an unresolved problem in many other areas such as environmental pollutants, agricultural biocides, etc. A key aspect to the problem is that the quantities or concentrations to which humans are exposed in the real life situation are many, many times lower than the quantities needed to produce effects in the animal test

Slide 19
Exposure
mice-men

systems). The mouse skin test is far removed from the human situation. None of the straight smoke inhalation tests have produced cancers. And none of the chemicals found in smoke are at concentration levels posing the hazard of toxic effects in humans.

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prestigious

*the prestigious
British
publication*

Professor of Biophysics P. R. J. Burch (in the April 5th issue of Lancet) expresses this opinion: "The relevance to man of animal studies, which have shown, for example, that the condensate from small cigars is much more carcinogenic than that from cigarettes, is very dubious... In my view, the evidence does not justify any attempt to produce a noncarcinogenic product."

Despite these difficulties, the search for less biologically active smoke is continuing. *with even greater expenditures of energy and money.* The justifying rationale very clearly is that the animal tests are relevant to human experience and that toxicity at high concentrations indicates possible long term risk at low concentrations.

Slide 20

Chem. Cos.

On this basis several large chemical concerns have joined the search for smoking material that would supposedly be "not so harmful" as tobacco. The proposed nontobacco materials are of two types: First, film-like sheets made of largely inorganic material producing so little tar that qualitative differences in biological effects of the tar are not important. An example of this type is the product Cytrel made by Celanese,

Slide 21
Cigts.

The second type is composed of partially pyrolyzed organic combustibles which do produce tar but of low biological effect. New smoking material (NSM) being produced for Imperial Tobacco Company

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^{second} is an example of this type. The theory behind this approach is that tobacco in its chemical composition is hopelessly complicated and results in an impossibly complex mixture of chemical constituents in the smoke. It was felt that by starting with a simple material such as pure alpha-cellulose, ^{or wood pulp} one could obtain smoke which is more controllable in composition and less likely to be biologically active.

With the impending introduction of several nontobacco smoking materials in British cigarettes, the Minister of Health in Great Britain established a group of experts, known as the Hunter Committee, to set procedures and to aid in the evaluation of test results/so that any new products introduced to the public would not only be supposedly less hazardous than tobacco, but would also at the same time not introduce new dangers.

The smoke of the nontobacco material either alone or/in mixtures with tobacco/differs substantially from the smoke of tobacco alone. It is not possible to predict the consequences of these changes in smoke composition. Tobacco has been smoked for hundreds of years. With the nontobacco smoking materials long term effects are unknown. So, if we are to use them we are faced with the question "Are we generating hazards to health not now in existence?"

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Slide 23
Bar Graph

NSM
Explain

Both Cytrel and NSM are now being extensively tested in the major research laboratories concerned with this problem as well as by some cigaret manufacturers who are contemplating their possible usage. The results of these tests, surprisingly enough, are showing that when admixed with appreciable quantities of tobacco the nontobacco smoking material offers little or no potential advantages. In the first place, it has a very bad off-taste so that regular tobacco smokers will reject it. Secondly, it does not reduce biological activity unless the proportion of the nontobacco material to tobacco is very high. In fact some proposed nontobacco materials have been found to be even more active biologically than tobacco and more active in admixtures with tobacco than either component alone. The mouse skin painting data on this graph are from the National Cancer Institute report to be published later this year.

Note 100%
NSM is
not
smokable

Slide 24
Ways to
reduce tar
& nicotine.

- It is true that the nontobacco smoking materials generally will reduce the tar and nicotine deliveries of the cigaret, thereby acting as a tobacco diluent. But less tar and nicotine from tobacco itself can also be achieved by the use of already existing techniques. I refer to efficient filtration, air dilution, to the use of expanded tobacco, and the use of tobacco filler modification through reconstitution processes. All of these techniques when properly employed can produce cigarets as low in tar and nicotine as any customer will ever want. It can be done without the

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use of nontobacco smoking materials of unknown long term effects. In short, there are many things our industry can do to reduce tars without making a synthetic cigaret.

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One of the disadvantages of NSM is the fact that it increases the generation of carbon monoxide in the smoke. Technically and healthwise this increase is not a problem because there is abundant evidence that in practically every conceivable situation/the human tolerance to cigaret smoke limits to a very safe level his exposure to carbon monoxide from the cigaret. The anti-cigaret nonsmokers have, however, made carbon monoxide (as well as discomfort factors) an emotional issue. The German Cigarette Association has recognized it to the extent of supporting research to reduce ^{carbon monoxide} CO generation from cigaretts. This problem could easily become a matter of concern to the American industry.

Slide 26
Old Lady

The cigaret industry, besieged as it is from many directions, has been so busy defending itself that it has, in my opinion, largely neglected the positive side of smoking. And there is a positive side as this picture shows. Relatively little research support has been given to this side, either by the companies or through the Council for Tobacco Research. The situation is similar in other countries. I was, therefore, delighted and pleased to read last Friday that on April 11th, Nobel Prize winner Professor Ulf von Euler, speaking to the Medical Expert Council of the Swedish Tobacco Company, made the following statement:

Slide 27
Cartoon

"Nobody would believe that so many people would use tobacco

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or products containing substances similar to nicotine, unless it had some positive effects.....It is surprising that research has dealt with this to such a small extent." Professor von Euler then went on to propose a biochemical mechanism for the action of nicotine on the nerve processes in the brain. This mechanism is suggested to explain the smoker's increased capacity to assimilate information and improved well-being. He cited experiments in which certain animals spontaneously prefer a weak nicotine solution as an alternative to drinking pure water.

Incidentally this cartoon is taken from a French picture story on "The History of Tobacco." The original French caption translates to the following: "It is remarked that never is a crime committed with a pipe or cigar to the mouth. Tobacco is then a moralizer or improver."

As some of you know, the positive side of smoking has received some attention from scientists at the Philip Morris Research Center.

Two years ago we helped organize a conference on the benefits of smoking as shown by the behavioral characteristics of smokers. In recent studies several investigators are finding more and more evidence that cigaret smoking reduces the arousal and/or aggressive tendencies of people in stressful situations. To conclude this presentation I would like now to show you a 5-minute video tape of the effect of nicotine on the violent tendencies of one of our subjects known as Jelly Bean *being, a cat*.

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Dunn book

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being studied under a grant to the Department of Psychology at Ohio State University. The tape is narrated by Professor Berntson who will explain the experiment.

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