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PERSONAL & CONFIDENTIAL

To: . Mr. W. McDowell

Date: January 27, 1983

From: . T. S. Osdene

Subject: . Smoking and Health, A Look Into The Future

I believe, that over the next two years, we will see a definite increase in attacks on both the smoker and on smoking itself. While some of these attacks will be based on so-called "scientific data", much of this criticism will be innuendos and invalid conclusions based on partial, selective scientific data. It is extremely difficult to separate scientific problems from those which are political in nature. Nevertheless, some of these controversies do present an opportunity for our industry to respond in a sound and intelligent manner.

The key issues, as I see them, are outlined below. Each of these will be examined and where feasible, some possible responses will be suggested. While some responses should involve the entire industry, in other instances, it might be more effective for PM to exercise leadership or respond alone.

1. Ambient Smoke and Passive Smoking Issue
2. Sidestream Components Issue
3. Issue of Improved Methods of Measuring Exposure Levels
4. Issue of Smoking in Women
5. Issue of Behavioral Effects of Smoking
- * 6. Issue of Compensation in Smokers of Low Tar Cigarettes
7. Issue of Interaction of Smoke with Heavy Metals
8. Issue of Smoking and Radioactivity
9. Issue of Effects of Smoking on Immune System
10. Issue of Smoking and Human Fertility
11. Issues of Drug Interactions in the Smoker
12. Tobacco Additives Issue
13. Issue of Effects of Smoking on Human Biological Systems

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14. Issue of Improved Analytical Methodology
15. Issues Related to Mechanisms of Alleged Smoke-Induced Diseases
16. Political Issues
17. Other Issues

1. Ambient Smoke and Passive Smoking Issue

- A. Continuing studies on the interaction of smoke with dusts such as coal, cotton, and grain are likely to show that smoking acts synergistically to increase the harmful effects of exposure to noxious dusts in the environment.
- B. The possible synergistic effects of smoking and exposure to industrial chemicals and pollutants in relation to the occurrence of respiratory diseases and various types of cancer will be investigated.
- C. Studies, such as those done by Hirayama, Trichopolos, and Froeb and White will attempt to show statistical correlations between exposure to smoke and diseases in the non-smoker.

Possible Responses to Ambient Smoke Issues

- A. Studies should be done to determine if the synergistic effect of smoking with environmental dusts holds true only for unique individuals who have an increased susceptibility because of prior conditions such as poor ventilatory capacity or chronic respiratory disease. These kinds of studies should be endorsed by the Industry. Animal studies done by Battelle Northwest failed to show this synergistic phenomenon with smoking and metallic dusts.
- B. Any criticism of the statistical findings of Froeb and White will strengthen the Industry's position.

2. Sidestream Components Issue

- A. Various components of sidestream smoke, especially nitrosamines and carbon monoxide, will be studied intensively as indoor air pollutants. Many investigations will focus on the possible injurious effects of sidestream smoke on the nonsmoker, especially children and compromised persons with impaired cardiac and pulmonary function. Unfortunately, alternative heating sources such as woodstoves and kerosene heaters and tightly insulated homes tend to exacerbate the effects of all indoor air pollutants.

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Possible Responses to the Sidestream Components Issue

- A. The "no effect" dose of ambient smoke over a long period of time should be determined experimentally in animals. Levels of dosages should be related to specific chronic exposure conditions for humans. The Tradescantia plant mutation assay used by EPA to monitor the possible mutagenic effects of ambient air pollutants should be applied to cigarette smoke.
 - B. Emphasis should be placed on the quick recovery experienced by even compromised persons to ordinary exposure levels of ambient smoke. The need for effective ventilation to reduce the levels of all indoor air pollutants in tightly insulated homes should be brought to the attention of the consumer.
 - C. Determination of the concentration of certain substances such as nitrosamines and other agents in ambient smoke and possible pathways of their decay should be conducted. The fate of smoke aerosols and their decay in different types of environments should also be examined.
3. Issue of Improved Methods for Measuring Exposure Levels
- A. More accurate dosimetry will be developed to measure actual exposure levels in humans to certain smoke components or under certain types of environmental conditions. In addition, animal studies will be utilized to experimentally determine exposure levels. Along with the above, personal monitors will be used to accurately measure human exposure to particulates, HCN, carbon monoxide, etc.
 - B. Methods of measuring nicotine in biological fluids in nanogram amounts or less will be developed.

Possible Response to Issue of Exposure Level Measurement

- A. The Industry should promote studies on the determination of smoke components and their decay products in ambient air. Without such accurate determinations, the industry will be pilloried by false innuendos.
4. Issue of Women and Smoking
- A. Smoking mothers and the effect of smoking on the unborn fetus will receive much attention. The effect of maternal smoking on infant and child development will be a major focus in this issue.

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- B. Transplacental carcinogenesis and teratogenic effects will be explored experimentally using animals exposed to smoke.
- C. New biological techniques will be devised and used to demonstrate the possible relationship of smoking to fetal defects.
- D. Experimental and epidemiological studies will evaluate all aspects of smoking in women. Women seem to show the greatest resistance to smoking cessation treatments. If the incidence of lung cancer is shown to exceed the incidence of breast cancer in women, a major controversy will ensue, with opponents to the industry attacking vigorously through the media.

5. Issue of Behavioral Effects of Smoking

- A. Studies will be conducted to show the alleged "addictive quality of smoke". The conventional wisdom, particularly among psychologists, is that smoking is addictive and nicotine is the responsible component. Based on this assumption, investigators will attempt to show that low delivery cigarettes are not less hazardous and that the manner in which they are smoked negates the perceived implication of a "safer" cigarette. This could lead to agitation for changing the FTC smoking parameters. Long-term animal studies on behavioral as well as tumorigenic end points related to nicotine dose levels are likely to continue. Other physiological studies in animals using opioid blocking agents (e.g. naloxone) will attempt to delineate a mechanism for the "addictive" nature of of cigarette smoking.

Possible Response to the Issue of Behavioral Effects of Smoking

Emphasis should be placed on the imprecise and misleading use of the term "addictive". It should also be stressed that recent studies show no physiological dependence to nicotine (e.g. DeNoble et al).

6. Issue of Compensation in Smokers of Low Tar Cigarettes

- A. Studies will be done to demonstrate that nicotine titration and compensation occur in smokers who smoke low tar cigarettes. It is quite probable that these studies will be poorly designed from a technical point of view, but will be carried out to prove some preconceived notions.

7. Issue of Interaction of Smoke with Heavy Metals

- A. Cadmium, chromium and nickel in tobacco and smoke will be investigated in various biological systems. Correlations between carcinogenesis and

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metal content in smoke will be determined and used to exert pressure on the Industry to remove these metals from tobacco. New theories of lung cancer induction will be based on heavy metal content of smoke and the results of heavy metal inhalation studies in animals exposed to heavy metals.

- B. The total burden of heavy metals in the environment will be calculated and used to show that heavy metals in smoke could be a major contributor to various pathogenic states.

8. Issue of Smoking and Radioactivity

- A. This subject, particularly Polonium-210, seems to reappear with alarming frequency. While little sound data is being developed by the scientific community, this issue does have tremendous appeal in the press.
- B. Further studies on the radioactivity issue will:
 - a. analyze lung tissue of smokers and nonsmokers who have died from lung cancer for Polonium-210.
 - b. produce lung tumors in experimental animals who are exposed to smoke treated with Po-210.
- C. Radon daughters, type and level, will be analyzed in inhalation studies using smoke-exposed and nonexposed animals. The possible attachment of Radon daughters to smoke aerosol particles of indoor air and their subsequent inhalation by both active and passive smokers will also be an issue.

9. Issue of Effects of Smoking on Immune System

- A. The effects of smoking on the immune system in humans will be evaluated. The relationship between increased IgE levels in smokers and greater susceptibility to respiratory diseases and lung cancer will be explored. The question of whether smoking impairs cellular immunity and depresses resistance to the alleged effects of promoters and carcinogens present in smoke will be addressed.

Possible Response to Issue of Smoking and Immune Effects

- A. The study of the effects of smoke on the immune system may be a method for identifying the "susceptible" individual and hence confirm the "constitutional" or "genetic" hypothesis which the Industry favors.

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10. Issue of Smoking and Human Fertility

- A. The effect of smoking on human fertility will be studied with emphasis on sperm production and sperm morphology in males exposed to smoke.

11. Issue of Drug Interactions in the Smoker

- A. Investigations on drug interactions in the smoker, particularly anesthetics, tranquilizers, and others will be carried out. Differences in effective drug dosage in smokers as compared to nonsmokers will be determined.

Possible Response to Issue of Drug Interactions in Smoker

- A. The major factors in variation in drug response include differences in rate of disposition of a drug at a particular organ site, genetic factors, emotional factors, etc. Smoking is commonly acknowledged as only a minor factor in variation in drug response.

12. Tobacco Additives Issue

- A. There is no doubt that DHHS will establish a system of biological evaluations (including transplacental carcinogenesis) for any new tobacco additives (both the additive and its pyrolysis products). The possibility of creating a government approved additives list exists. The focus of this issue will be on appropriate analytical methods for detecting and identifying additives and their pyrolysis products.
- B. Periodic outbursts over coumarin, cocoa, etc. will occur in the press and the Industry will be placed in the position of defending these issues. As a result, we may have to do more extensive biological testing of substances presently in use in order to discredit the opponents' arguments.

13. Issue of Effects of Smoking on Human Biological Systems

- A. The effect of smoke on lung clearance and lung alpha-1 anti-trypsin will be used to show that smoking may be responsible for emphysema. The mobilization of macrophages and leukocytes will be investigated in smokers, with special emphasis on the release of the enzyme elastase in the lung.
- B. Studies will be conducted to determine the effects of smoking on the production of prostaglandins. Attempts will be made to relate prostaglandin levels to the cardio-pulmonary effects attributed to smoking.

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Further, prostaglandin biochemistry may be involved in the phenomenon of tumor "promotion".

14. Issues of Improved Analytical Methodology

- A. Improvements in the analytical methodology used to determine the concentrations of nicotine, cotinine, thiocyanate and other smoke metabolites in biological fluids will be made. Nanogram levels of detection of these metabolites will become routine. These techniques will be used to measure smoke metabolites in the "ambient smoke" controversy. Attempts to detect these metabolites in amniotic fluid will also be pursued.

15. Issues Related to Mechanisms of Alleged Smoke-Induced Diseases

- A. Although it is unlikely that any new diseases will be added to the list of those which are allegedly related to smoking, much so-called basic research will be devoted to developing disease models to demonstrate the mechanisms by which cigarette smoke causes certain diseases. In addition to animal models, in vitro tests will also be utilized. Studies designed to explore mechanisms of smoke damage in human cells will become increasingly more complex and will become more biochemically oriented.

16. Political Issues

- A. Political issues cannot be ignored since they have a substantial impact on the scientific arena in which the smoking and health controversy resides.
- B. More industries will attempt to absolve themselves of responsibility and attribute their industrial hazards to smoking (e.g. asbestos, cotton, and coal mining industries, among others).
- C. The pressure to produce an acceptable self-extinguishing cigarette will increase, regardless of other aspects of such a product, including taste, tar delivery, etc.
- D. Smoking cessation programs will increase. Taxation will be used as a source of revenue and as a deterrent to smoking.
- E. The major thrust of the opposition will be towards conveying the social undesirability of smoking. Thus the smoker may be perceived as a social outcast or as an uncaring, socially irresponsible individual. The message to be conveyed to the public is that smoking behavior may be considered as deviant.

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- F. In the Third World, we will see increased efforts towards smoking cessation, and attacks on the health, economic, and financial implications of smoking in those countries will increase. WHO in Geneva will lead many of these efforts against smoking and the tobacco industries.
- G. Attempts to misrepresent Industry arguments will continue to the detriment of the Industry and this should be anticipated.

17. Other Issues

- A. More companies will discourage smoking and will institute smoking cessation programs. This is because studies have shown that the worker who smokes is absent more frequently and that smoking causes excess cleaning problems in factories and offices.

Insurance companies are granting lower rates to nonsmokers. The zealous nonsmoker is demanding a smoke-free working space and the courts are maintaining this as a right which must be granted.

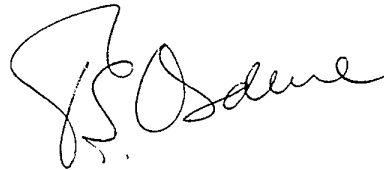
Workman's compensation is involved. Compensation has been awarded for the perceived harmfulness of being exposed to ambient smoke. Awards in "black lung" cases have been denied because the miner was a smoker. There are analogous cases for byssinosis.

In the above analysis I have not pulled any punches and in many instances the issues are addressed from the perspective of our opposition. I believe that a number of these issues can and should be addressed, particularly those where we stand a high probability of success in generating solid data which can be used in the scientific/PR forum. Thus, this document should be viewed as a realistic appraisal of challenges and opportunities which we face. A long-term commitment toward these goals should enable our industry to continue to thrive in the future.

I shall be glad to discuss these issues with you in greater depth at your convenience.

TSO/pw

cc: Dr. Max Hausermann



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