For Presentation at a White House Briefing on the Reduction of Tobacco Caused Disease

July 23, 1997

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Tobacco use causes one fifth of all deaths in our nation and produces unparalleled suffering, disability and lost productivity. We have a historic opportunity to change the course of our nation's health. Among the many issues and considerations, two define our challenges:

(1) On our current course, between 10 and 20 million current cigarette smokers will prematurely develop debilitating disease, suffer and die, because of their unmitigated tobacco use. We have effective treatments that could help many of these individuals, but we need new treatments and strategies to help those refractory to current approaches.

(2) Implementation of proposed strategies to reduce access and appeal of tobacco products could reverse the current trend of increased youth tobacco use; however, even under the most optimistic projections, more than 500,000 kids will continue to develop nicotine addiction every year. Further research is needed on the etiology of the addictive process if we are to make lasting progress.

If we are to set our nation on a course of reduced tobacco caused death and disease, the following strategies are fundamental to consider.

(1) Our national tobacco and nicotine research agenda must be substantially expanded to complement and support any settlement processes: Supportive, integrated and complementary research is essential across a variety of disciplines. There is compelling need to expand our research in least four areas, if we are to maximize the immediate benefits of scientific findings, minimize the undesirable consequences of ongoing tobacco use and its initiation, and embark on a course that produces an increased capacity to reduce tobacco-related death and disease. Three federal agencies—the Centers for Disease Control and Prevention, Office on Smoking and Health (CDC, OSH), the National Institutes of Health (NIH), and the Food and Drug Administration (FDA)—that already play key roles in coordinating and overseeing such research could be encouraged (and of course, funded) to expand their current work.

   a. Surveillance Research (CDC,OSH): Rapid, responsive and much more comprehensive monitoring of the use of all forms of nicotine is necessary to provide mid-course policy corrections, to guide regulation, and to enable more rapid dissemination of new treatment approaches.

   b. Basic Research (NIH): Research on the pathophysiology and development of nicotine dependence is critical to provide the basis for continuing improvement in prevention and treatment efforts.

   c. Prevention and treatment research (CDC, OSH and NIH): We are fortunate that many tobacco-addicted people can be effectively treated along the guideline issued by the Agency for Health Care Policy and Research. However, both CDC and NIH research in this area must be expanded if we are to embark on a course that will take us to continuing reduction of tobacco-caused death and disease. Initial research leading to the development of nicotine patches came from the National Institute on Drug Abuse (NIDA). NIDA and other national institutes have been helping support the research that has already led to improved efficacy of use with both the nicotine patch and gum. Such research complements valuable work being done by the pharmaceutical industry.

   d. Regulatory Research (FDA): The regulation of tobacco and nicotine is well within the purview of the FDA. Yet the agency will be hamstrung in many areas vital to progressive regulation if it cannot ensure that research on topics ranging from cigarette dose evaluation, labeling and the thresholds of various consequences of tobacco uses (e.g., addictive levels of nicotine) is systematic. Such systematic study would complement work done at NIH and be no less vital to the public health.

(2) Reduction of tobacco toxin exposure could be an important component of our national efforts to reduce the death and disease caused by unmitigated tobacco use: Then again, it might not; this depends on how an exposure reduction scheme is implemented and on the rules of its implementation. Ameliorating smoking-related death and disease by reducing smokers' exposure to tobacco toxins is consistent with the finding of many major studies, Surgeon General's Reports, and a 1997 NCI monograph. David Burns (the editor of several Surgeon General's Reports) developed a model predicting that depending on his or her age, baseline cigarette smoking, and magnitude of smoking reduction, a smoker might enjoy an increase in life expectancy ranging from approximately one month to 5 years. On the other hand, the aggressive marketing of theoretically low-tar cigarette brands by tobacco companies led to an apparently increased risk of lung cancer and reduced motivation of the users of these cigarettes to quit smoking.

We should discourage tobacco companies from selling cigarettes made more toxic than necessary, and we should encourage pharmaceutical companies to develop products and indications that serve the many smokers who are currently unwilling or unable to completely abstain from tobacco use. Attached is a set principles for exposure reduction approaches that could be applied to all forms of nicotine delivery.

In developing a research agenda, I would encourage you to take advantage of research organizations such as the Society for Research on Nicotine and Tobacco (SRNT), the College on Problems of Drug Dependence (CPDD), and the American Psychological Association (APA).

(3) Regulation of all nicotine delivery products must be consistent with their addictive profile and overall toxicity. There has been much talk of the need for a "level playing field" for nicotine products, be they drugs from pharmaceutical companies or cigarettes and snuff from tobacco companies. Our goal should be to undo and reverse the present regulatory paradox, whereby the most addictive and toxic forms of nicotine delivery are marketed more liberally than life-saving nicotine replacement medications. We should be taking every possible step to decrease demand for the most toxic products, provide incentives for developing nicotine dependence medications, and stay headed in the direction of reduced tobacco-related tolls. Cigarettes should be as safe as current technology allows them to be, without claiming for themselves any objective safety, since all forms of smoking incur marked risks. Safer forms of nicotine delivery should be touted, especially when they are paired with smoking cessation and weaning programs. Improvements in the nature and use of nicotine medication should be stimulated, not stifled.

For Discussion at the Conference on " Alternative Nicotine Delivery Systems: Harm Reduction and Public Health"

March 21-23, 1997
Toronto, Canada

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Exposure Reduction by Partially or Fully Substituting Safer Forms of Nicotine Delivery for Cigarettes

The observation that the toxicity and addictiveness of nicotine varies widely as a function of the dosing characteristics and other constituents of nicotine delivery system raises the possibility that alternate forms of nicotine delivery could be fully or partially substituted for cigarettes. In principle, both tobacco and pharmaceutical companies could market such products and/or applications of nicotine delivery products to achieve this end. However, the degree to which individuals and society as a whole benefit from such nicotine product use might depend as much on the actual patterns of product usage as on the products themselves.

The following draft principles and questions to ask of tobacco exposure reduction efforts is an attempt to develop strategies that might lead to genuine tobacco exposure reduction and reduction of both individual and overall tobacco exposure.

I. Basic Principles for Exposure Reduction Products and Strategies

1. The purpose of the indication or product must be to reduce the death and disease caused by tobacco.

2. The long range goal for the indication or product should be to leave smokers both tobacco- and nicotine-free.

3. It should pose no added safety risk and safety data should be extensive, including data on extended use.

4. The indication or product should not worsen the individual's level of nicotine dependence.

5. It should not reduce the likelihood of eventual cessation of tobacco use.

6. The indication or product should not lead to increased population prevalence of nicotine dependence.

7. It should not appeal to adolescents or increase the risk of adolescent misuse or abuse.

8. Marketing for the indication or product should provide consistent smoking cessation messages and offer help in quitting as well as help in terminating use.

It is important to note that these principles do not embrace the premise that nicotine dependence itself is inherently benign and that the only goal is to lessen the risk incurred, regardless of whether the prevalence of dependence is increased. The ultimate goal is for individuals to be tobacco- and nicotine-free to the greatest possible extent.

Questions to be Asked of All Indications or Products

In addition to the principles above, there are questions which could be applied to any product/indication, whether developed by a pharmaceutical company or the tobacco industry, to help insure the principles are upheld. These might include:

1. What is the intended or predicted patterns of consumer use?

2. What are the short term and long term safety/toxicity data?

3. What are the nicotine delivery characteristics?

4. What are the abuse liability and dependence potential characteristics?

5. What are the potential immediate and long term health effects for individuals?

6. What are the potential immediate and long term health effects at the population level?

7. What constituents other than nicotine are delivered to the user?

8. What are the standards for evaluation of health effects?

9. What are the regulatory issues posed by the product/indication?

10. What level of post marketing surveillance is required?

11. What is the likely effect of this indication/product on the prevalence of nicotine dependence?

These principles and questions provide a framework for careful consideration of the intent, design, and impact of an indication or product. They should be validated by scientific and regulatory experts and consistently applied to all potential uses.

From: Jack Henningfield
July 7, 1997
From Presentations to NIDA
Extramural Advisors and Council, 1994

CHALLENGES TO NIDA NICOTINE RESEARCHERS

- COGNITIVE EFFECTS & BRAIN MECHANISMS
- CO-MORBIDITIES
- DIAGNOSIS AND TREATMENT
- MEDICATIONS DEVELOPMENT
- PREVALENCE: SOCIETAL DETERMINANTS
- YOUTH

COGNITIVE EFFECTS OF ADMINISTRATION/WITHDRAWAL

- Role in dependence process
- Time course (onset and offset)
- Types of cognitive effects
- Individual differences
- Brain mechanisms

PREVALENCE: SOCIETAL DETERMINANTS

- Factors that might be manipulated
  e.g., cost, alternative options, education
  treatment availability

- A model for other drug abuse

YOUTH

- Evaluate risks and benefits of "adult treatments"
  - Pharmacologic
  - Behavioral

- Developmental factors that alter vulnerability
  - hormonal interactions?
  - weight control?
  - cognitive?
  - mood control?

A pediatric approach may be essential (i.e., build on adult knowlege base and extend to youth).

CO-MORBIDITIES (SUBSTANCE AND AFFECTIVE)

- Etiology
  - predictors of vulnerability
  - mechanism of interaction
- Treatment
  - effect on prognosis
  - treatment strategy

DIAGNOSIS AND TREATMENT

- Primary care diagnostic instrument needed
  - DSM & FTQ provide complimentary non identical data
  - Other relevant factors (e.g., co-morbid conditions)
  - Individualized sources of reinforcement
- Cost effectiveness

MEDICATIONS DEVELOPMENT

- Alternate nicotine replacement systems
  - adverse vs. beneficial effects
  - maintenance systems: risks and benefits
- Selective nicotinic agonists and antagonists
- Non nicotinic acting agents

JAN 8, 1982

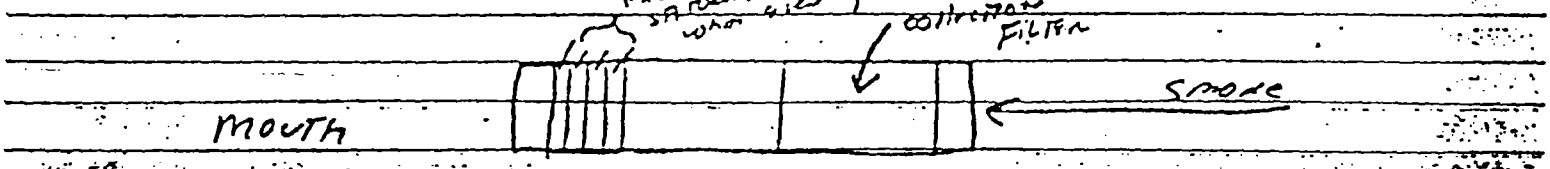
TO: Jim Charles

From: V.I. DeNoble

Jim:

In Response to our Meeting on January 7, 1982, I would like to suggest the following Idea.

Develope a multiple phase filter that will Remove many gas phase components from smoke. The same filter at the proximal end to the mouth have a series of pads with the components that you wish to Add to Smoke.



Vic DeNoble

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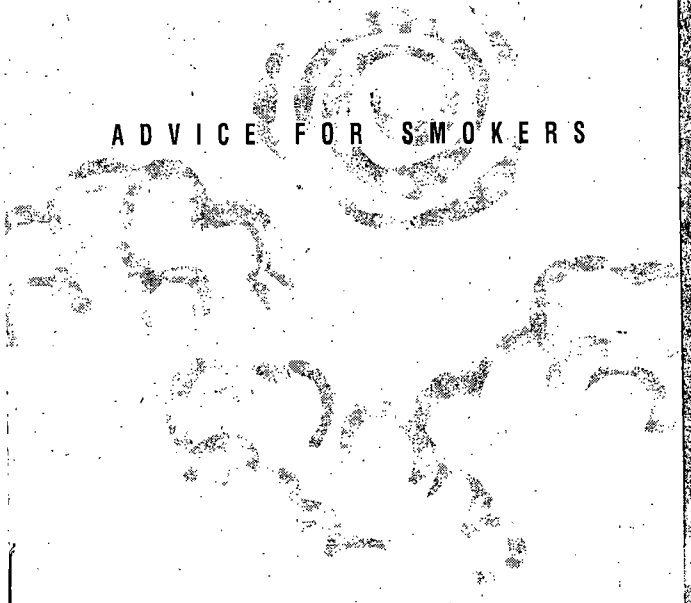
LOW TAR CIGARETTES ARE HAZARDOUS TO YOUR HEALTH

ADVICE FOR SMOKERS



ARF Addiction Research Foundation
Fondation de la recherche sur la toxicomanie