



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20892

July 11, 1997

TO: Harold Varmus, M.D.
Director, NIH

FROM: Director, NCI

SUBJECT: Tobacco-Related Biomedical Research Trust Fund

Goal:

The goal of this research Trust Fund is to provide substantial funding to allow the Nation to make progress towards reducing the burden of tobacco and tobacco-related disease via:

- a) Research into the use and direct effects of tobacco and tobacco products
- b) Research into reducing the burdens of tobacco-related diseases

Size of the Trust Fund:

In order to make a significant and sustained impact towards reducing the terrible toll exacted by tobacco use and addiction, we need to provide an amount of research funding commensurate with the enormous burden of disease and disability that tobacco causes. If we assume that 20 to 25 percent of the death and disability in this country can be related to tobacco and that our current investment in research aimed at alleviating all disease is approximately \$13 billion. We estimate a need of approximately \$3 to \$3-1/2 billion per year.

Principles:

- a) This Trust Fund should provide for a stable source of funding over long periods of time. For that reason, we propose a mechanism whereby the principal of the Trust Fund is able to be invested so that the income on the investment grows in order to provide \$3+ billion a year in stable research funding. The stability for the long-term investment that will be required should entail a protection of the principal, once the fund reaches the capacity to sustain a steady state funding level. Details of the rate of growth and disbursement of funds will require further modelling to achieve the funding goals.

How much already being spent

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- b) The Trust Fund should be used to address the full range of tobacco-related and tobacco-related disease research and the research must be of high quality. To optimize the assurance of high quality and so as to not reinvent funding mechanisms, the Trust Fund income should be funneled through the US Government to be further distributed among well established research structures within the government, including NIH, CDC, AHCPR, VA, etc.
- c) In order to assure that the funds are used to achieve an agreed upon program of tobacco-related and tobacco-related disease research activities, an independent periodic review and set of programmatic recommendations should be made by a disinterested body of experts convened by a neutral entity such as the National Academy of Sciences. A three-year review would provide an evaluation of the fund activities and recommend how the funds should be distributed across programs, scientific and medical needs and opportunities, as well as across agencies. Such a regular review should assure the public of the proper use of the funds.
- d) There should be a separate and distinct accounting of the Trust Fund monies to assure that they represent supplements to the Nation's investment in tobacco-related and tobacco-related disease research activities and that these supplements fulfill the special goals of the Trust Fund.
- e) An attempt should be made to formulate a mechanism to protect the appropriation process for PIIS research agencies so that Trust Fund monies do not serve to replace appropriations. For example, no agency can receive monies from the fund in any fiscal year, if they do not receive an appropriation for research equal to or greater than the previous year's appropriation.
- f) A Presidentially-appointed Board of Trustees would oversee the investment and fund disbursal of the Trust Fund monies and assure that the quality control processes for independent review and program recommendations take place. This Board would be responsible for implementing the recommendations of the outside review panel, and charging that panel(s) with future review requirements.

How to ensure displacement not done

Richard D. Klausner, M.D.



NIH Plans for the Public Health Trust Fund for Research on Tobacco Use and Tobacco-Related Diseases

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I. PREFACE

The NIH mission is to uncover new knowledge that will lead to better health for everyone. This knowledge is aimed at helping prevent, detect, diagnose, and treat disease and disability ranging from rare genetic disorders to the common cold. As part of the fulfillment of this important mission, the NIH conducts and supports a wide variety of research related to tobacco and the diseases to which tobacco contributes. Tobacco-related research is particularly relevant to the missions of certain of the individual Institutes that are components of the NIH. These Institutes are: the National Cancer Institute (NCI); the National Heart, Lung and Blood Institute (NHLBI); the National Institute of Child Health and Human Development (NICHD); the National Institute of Dental Research (NIDR); the National Institute of Drug Abuse (NIDA); and the National Institute of Environmental Health Sciences (NIEHS). The relevance of tobacco to the missions of these Institutes is self-evident given that: 1) tobacco is a major causal factor in the four leading causes of death in the US (heart disease, cancer, stroke, and chronic obstructive pulmonary disease); 2) approximately 90% of adult smokers begin smoking as children, adolescents, or teens; 3) tobacco can have very deleterious effects on children passively exposed in utero and during infancy; 4) tobacco is a contributing factor to several serious oral conditions including cancers; 5) nicotine is a highly addictive drug; and 6) smoke from tobacco is a serious environmental hazard.

Representatives from each of the above Institutes and from the Office of the Director, NIH have contributed to the formulation of this document, which has a three-fold purpose. Firstly, the impact of tobacco on the health of the Nation and the consequent costs will be described. Secondly, the tobacco-related research within the portfolios of each of the Institutes will be briefly summarized. Finally, an attempt will be made to describe the vision of each of the Institutes regarding plans for the utilization of a Public Health Trust Fund (PHTF) that has been proposed as part of the recently announced Tobacco Settlement Agreement. Specifically, examples of the types of expansions of effort that could be enabled by the establishment of the PHTF will be provided in the context of their impact on the ability of the NIH collectively to combat tobacco-related diseases.

While the programs of each of the Institutes will be considered separately in this document, it should be stressed from the outset that tobacco use and tobacco-related disease are considered to be common enemies. While there may be some areas of overlap in the efforts of the individual Institutes to reduce tobacco use and the burden of tobacco-related disease, these are not seen as areas of competition but rather as opportunities for cooperation and collaboration. All of the Institutes that comprise the NIH are firmly committed to improving the health of the Nation. Perhaps nowhere is this resolve more pronounced than in the battle against tobacco use and tobacco-related diseases. The motivational basis of this mutual commitment is summarized in the next section of this document that describes the havoc that tobacco wreaks upon the health of the American people.

II. THE IMPACT OF TOBACCO USE ON THE NATION

This section is arranged as a series of bullet points that describe in various ways the impact of tobacco first in terms of morbidity/mortality and then in terms of the economic costs of tobacco to our society. Individuals are affected variably by these illustrations finding one or another of them to be either shocking or astonishing. Indeed, these descriptions of the impact of tobacco are intended to shock and astonish, because the devastation of tobacco is truly shocking and astonishing.

A. The National morbidity/mortality burden of tobacco use

- Tobacco kills over 430,000 of the US population each year, more than alcohol, cocaine, heroin, homicide, suicide, car accidents, fire, and AIDS combined. This death toll is about equivalent to a no-survivors plane crash with 200 persons on board occurring every 4 hours around the clock every day of the year.
- Tobacco annually kills more Americans than died in all of World War II, 8 times more Americans than died in the entire Vietnam war, 6 times more than die annually in accidents, and 20 times more than are murdered each year.
- During the 1990's tobacco will kill more than 4.5 million American—the equivalent of to losing every man, woman, and child in Portland, OR; Fargo, ND; Flint, MI; Buffalo, NY; Greensboro, NC; Miami, FL; Baton Rouge, LA; Austin, TX; Denver, CO; Berkeley, CA; Salt Lake City, UT; and Cleveland, OH, combined.
- Each day in the US, nearly 3,000 persons under age 18 start smoking. About 18 will someday die from homicide and 35 in car accidents, but 1,000 will die from a tobacco-related disease.
- 5 Million children alive today will die prematurely because of the decision to start smoking as adolescents, and on average, each would live 15 years longer if a nonsmoker.
- Smoking is a major contributor to the top four leading causes of death in the US [Heart Disease, Cancer, Stroke, and Chronic Obstructive Pulmonary Disease (emphysema + chronic bronchitis)].
- Of the smoking-associated mortality each year, approximately 180,000 deaths are from cardiovascular disease, approximately 150,000 deaths are from cancer, approximately 85,000 deaths are from respiratory diseases, nearly 2,000 are deaths among infants, and another nearly 1,400 people die in fires started by smoking.
- ★ • Lung cancer is the number one cancer killer in both men and women with over 150,000 in the US expected to die this year alone. Lung cancer kills more than twice as many men as prostate cancer, the number two killer in men and about the same as prostate, colorectal, pancreas, and lymphoma combined. Since 1987, more women have died each year of lung cancer than breast cancer, which for over 40 years, was the major cause of cancer death in women. In 1997, it is estimated that approximately 22,000 more women will die of lung cancer than of breast cancer. Within 5 years, twice as many women will die of lung cancer than of breast cancer.

- Use of smokeless tobacco (spit tobacco) is increasing especially among male adolescents and young male adults with as many as 20% of male high school students having used smokeless tobacco and 6% of males 18 years and older being regular users of snuff or chewing tobacco. In some populations, spit tobacco use is as high as 40%. Smokeless tobacco can cause cancer and a number of other oral conditions with nearly a 50-fold excess risk of cancer of the cheek and gum among long-time users. Smokeless tobacco also contributes to nicotine addiction that may manifest itself in smoking in addition to smokeless tobacco use.

- 9 out of 10 nonsmokers have a detectable nicotine metabolite in their blood indicating recent exposure to cigarette smoke; ~37,000 heart disease deaths and ~3,000 lung cancer deaths each year are due to second-hand smoke; one study indicates that being around people who are smoking, even as little as one hour a day, nearly triples a woman's risk of contracting breast cancer.

- Over 40% of children age 2 mo. to 11 yr. live in a home with at least one smoker; some estimates attribute 10% of all infant deaths to smoking by others; in infants under age 18 months, secondhand smoke is associated with as many as 300,000 cases of bronchitis and pneumonia; as many as 15,000 infant hospitalizations may be linked to second-hand smoke.

B. The National economic burden of tobacco use

- Smoking is responsible for approximately 7 percent of total US health-care costs

- For each of the ~24 billion packs of cigarettes sold each year, over \$2 are spent on avoidable medical-care costs (nearly \$50 Billion in total).

- Between 1987 and 1993, the direct costs of medical care attributable to smoking doubled.

- ~\$27 Billion of these smoking-attributable costs were for hospital expenditures, ~\$15 Billion for physician expenses, ~\$5 Billion for nursing-home expenditures, and ~\$1 Billion for home health-care expenditures.

- Of these costs, over 40% (~ \$20 Billion/year) are from public funds (i.e., Medicare, Medicaid, and other federal and state sources); for those over age 65, public funds accounted for more than 60% of the smoking-attributable medical-care costs.

- Even though they die at earlier ages than non-smokers, the current and former smokers generate an estimated \$500 Billion in excess health-care costs over their lifetimes.

- Each year, decisions by 1 million youth to become regular smokers commit the health care system to over \$8 Billion dollars in extra expenditures over their lifetimes.

- These cost estimates are underestimates in that they do not include burn care from smoking-related fires, perinatal care for low-birthweight infants of mothers who smoke, and medical-care costs associated with disease caused by second-hand smoke.

- Taken together direct and indirect costs of smoking is more than \$100 Billion/year or about \$4 for each pack sold in the US. Each minute, tobacco costs the American people about what we pay our President in salary for a year.

III. NATIONAL CANCER INSTITUTE (NCI)

The National Cancer Institute coordinates the National Cancer Program, which conducts and supports research, training, health information dissemination, and other programs with respect to the cause, diagnosis, prevention, and treatment of cancer, rehabilitation from cancer, and the continuing care of cancer patients and the families of cancer patients. Tobacco use is responsible for approximately one-third of all cancers. Foremost among the cancers caused by tobacco is lung cancer, which is the number one cancer killer in both men and women. While certain other factors (e.g., radon and asbestos) have been linked to lung cancer, far-and-away the most significant risk factor is cigarette smoking, which has been linked to about 90% of lung cancer cases. Over 500,000 cases of lung cancer are anticipated in the US in 1997 with over 90,000 men and over 60,000 women expected to die of the disease in this year alone. Lung cancer is among the most tragic of cancers in that it is largely preventable, and once contracted, current interventions are of very limited efficacy with 5-year survival of all stages combined being only 14%. In addition to lung cancer, mortality attributable to current and past tobacco use has also been linked to cancers at other sites including lip, oral cavity, pharynx, esophagus, pancreas, larynx, trachea, cervix uteri, urinary bladder, and kidney. Cancers at several other sites have also been suggested to be linked to tobacco use and these putative associations are currently under study.

The exposure to the cigarette smoke of others is also a significant issue. It has been estimated that 3,000 lung cancer deaths each year are attributable to exposure to the smoking of others (secondhand smoke). One recent study indicated that an exposure to even as little as one hour per day of secondhand smoke resulted in a nearly triple increase in a woman's risk of contracting breast cancer.

The NCI has been and will remain committed to reducing the burden of all cancers. In this document, the current portfolio of tobacco-related research supported by the NCI will be briefly summarized. In addition, examples of the types of research that could be enabled by the PHTF will be provided. The PHTF will represent a truly unique source of funding for cancer research. In planning for the use of these supplemental resources, the NCI believes that "big thinking" should prevail. Projects of a National scope whose sheer magnitude has previously taken them off our radar screens (because of funding limitations) ought now to be reconsidered. The NCI herein provides some examples of such projects. These include:

- Markedly increased funding for investigator-initiated tobacco-related research
- Expanded participation in clinical trials relevant to tobacco-related cancers
- Prevention of tobacco-related cancers for 45-50 million former smokers
- Development of preclinical models for tobacco-related cancers
- Exploration of cancer susceptibility and gene-tobacco interactions
- Improved early detection and diagnosis of tobacco-related cancers
- Improved National surveillance of tobacco-related cancers
- Improved communication about tobacco-related cancers and interventions

A. Tobacco-Related Research of the NCI

In FY96, the NCI supported a variety of research efforts related to tobacco and tobacco-related diseases. Smoking and health research totaled \$82M in FY96, which included behavioral research related to smoking, research related to smokeless tobacco, and the ASSIST program. Foremost among cancers caused by tobacco is lung cancer where

about 90% of cases are a result of exposure to primary or secondhand tobacco smoke. In FY96, the NCI sponsored over 500 grants with relevance to lung cancer (the actual degree of relevance to lung cancer varies from project to project as evaluated by the NCI), and the lung cancer portfolio of the NCI totaled approximately \$119M. In addition to lung cancer, mortality attributable to current and past tobacco use has also been linked to cancers at other sites including lip, oral cavity, pharynx, esophagus, pancreas, larynx, trachea, cervix uteri, urinary bladder, and kidney. In FY96, each of these cancer sites was the subject of NCI-sponsored research; research support for head and neck cancer totaled ~\$35M; bladder cancer studies totaled ~\$15M; kidney and urologic disorders totaled ~\$111M; esophageal cancer studies totaled ~\$7M; pancreatic cancer research totaled ~\$8.5M; larynx cancer research totaled ~\$1M; cervical cancer and uterine cancers research totaled ~\$60M. Cancers at several other sites have also been suggested to be linked to tobacco use and these putative associations are currently under study. The scope of NCI-sponsored projects in all of these cancers encompasses basic research at the molecular level, clinical and behavioral research, chemoprevention, surveillance and epidemiology, and applied research at the community level.

Categories of research supported, and examples of tobacco-related research within each category, include:

- Molecular/Genetic Studies (e.g., Carcinogen metabolizing enzymes and head and neck cancer; Molecular epidemiology of lung cancer; Genetic analysis of transformation of human fibroblasts; P53 marker for oral cavity premalignancy and cancer risk)
- Tobacco-Related Carcinogenesis Studies (e.g., Mechanisms of bladder tumorigenesis; Isothiocyanates and nitrosamine carcinogenesis; Experimental tobacco carcinogenesis; Dibenzo(A,1)pyrene - tumor initiation and promotion)
- Chemoprevention Studies (e.g., Chemoprevention of aerodigestive epithelial cancers; Phase II trial of Anetholtrithione (Sialor); Lung cancer chemoprevention program; Preclinical toxicology of chemopreventive agents; Chemoprevention of head and neck cancers)
- CARET - Carotene and Retinol Efficacy Trial
- Epidemiology Studies (e.g., Ecogenetic study of lung cancer in minorities; Genetic and environmental risk factors for bladder cancer; Epidemiology of glutathione transferase and lung cancer; Determinants of teenage smoking behavior; Occupation, ETS, and lung cancer in nonsmoking women)
- Clinical Intervention Studies (e.g. Smoking cessation, weight gain, and exercise in women; Indigent care hospital-based smoking cessation program; Smokeless tobacco - nicotine patch and self-help treatment; Reducing maternal smoking at the pediatric health visit; Interactive videodisc smoking cessation intervention; Effectiveness of nicotine patch adjuvants)
- Community Intervention Studies (e.g., Smoking prevention through a combined mass media and school program; Strategies for smoking cessation among low-income women; Legal interventions to reduce tobacco use; Mediators of worksite cancer prevention effectiveness; Tobacco farmers and tobacco control; Effectiveness of community initiatives to limit teenage access to tobacco)

- ASSIST - American Stop Smoking Intervention Study for Cancer Prevention (a trial of a protocol developed by NCI to reduce mortality from cancer caused by tobacco involving more than 6,200 organizations in 17 states)
- PLCO Screening Trial (a health study involving 150,000 Americans to determine whether screening tests for prostate, lung, colorectal and ovarian cancers will reduce the number of deaths from these cancers)

B. NCI Plans for Expanded Tobacco-Related Research

An especially exciting prospect of the establishment of the PHTF is the ability to reach significantly beyond the types of research efforts that are possible under current funding limitations. It is to this prospect that the remainder of this document will be addressed. Each of the sections that follow represent projects whose sheer magnitude has previously taken them off our radar screens because of funding limitations. If the PHTF materializes, these projects of truly National scope would be enabled. These include:

1. Markedly increased funding for tobacco-related research

The PHTF with an appropriate level of funding would enable significant expansion of the approaches already included in the NCI's portfolio. The NCI holds investigator-initiated research as one of its highest priorities. However, current funding limitations restrict the number of meritorious grant applications that can be funded. The NCI currently has a success rate for grant applications of approximately 25%, and has made as one of its goals to raise this success rate to at least 40%. It has been anticipated that the process of accomplishing this goal would take several years of incremental increases in Congressional appropriations. The PHTF would enable the NCI to more rapidly increase the success rate for tobacco-related research. This would be accomplished through a series of carefully considered Request For Applications (RFAs) and through increased funding levels of investigator-initiated grant applications in this area. An innovative tobacco control research program is essential to guide new policies, regulations, and programs supported by public and private funds. Research must address issues at the national, state, local, and individual level, and must include studies of adult tobacco use and its impact on youth. Of particular urgency is the need for science-based information to inform federal and state policies and programs that are under development. Research is also needed to guide the public education campaign, the use of smoking cessation trust funds, and required changes in the corporate culture of the tobacco industry. Studies that span the spectrum from basic through applied research are needed. A comprehensive tobacco control research portfolio will contribute to real reductions in tobacco use only if it is linked closely to ongoing and expanded intervention programs.

With resources from the PHTF, the NCI would immediately propose to institute an exceptions program for grant applications relevant to tobacco and tobacco-related diseases whereby applications outside the NCI payline would be eligible for funding if their peer review priority score were within the top 40th percentile (for R01 applications). Analogous increases via exception funding would be formulated for non-R01 granting mechanisms (e.g., P01). These increased resources would enable research that would include an increased investment in basic research aimed at understanding tobacco and the biological mechanisms underlying the cancers caused by tobacco. One of the metrics by which progress in the fight against cancer is measured is an increased knowledge about cancer. Common sense would

Indicate and experience has proven that knowing the enemy is a key feature of a successful engagement.

The PHTF could also fund increased investment in methodologic and behavioral research to clarify the most promising research designs and strategies for prevention and cessation of tobacco use, particularly in populations where tobacco use has remained high, e.g., adolescents, women, certain special populations, and among those with less education and income. A comprehensive program aimed at tobacco control research would include new research aimed at understanding the initiation of tobacco use and nicotine addiction. Studies must also address questions related to racial, cultural, and gender influences in youth tobacco use including the impact of new, proposed, and future tobacco product regulations. It will be critical to assess via research the impact of new tobacco products ("less hazardous tobacco products" on initiation and cessation rates prior to the marketing of these products). While many teenage smokers have tried to stop, most do not succeed. Research is desperately needed to guide interventions in this important field. Clinical studies are needed to develop new treatment regimens including pharmacological studies of nicotine delivery devices and other drugs either separately or in combination with a variety of behavioral interventions. It will also be critical to assess the success of intervention programs and to develop the methodologies for this assessment. Using methodology developed as part of the NCI's ASSIST program allows the relative contributions of regulatory and program interventions to changes in tobacco use to be assessed. As new interventions are developed, new assessment tools will need to be developed in concert.

2. Expanded participation in clinical trials relevant to tobacco-related cancers.

For more than 30 years the NCI has supported a successful cooperative multicenter trials program in treatment and, more recently, in prevention. Operating at hundreds of sites in North America, NCI's cooperative groups have generated much of the evidence on which the practice of oncology is now based. It is also currently the platform for two very large trials aimed at the prevention of breast cancer and prostate cancer, respectively. The clinical trials program has always paid close attention to tobacco-related cancers, and active programs for cancers of the lung, bladder, head and neck, esophagus, kidney, and pancreas have been in place for years.

Some of the anatomic sites at risk from tobacco present special opportunities for intervention. The bladder mucosa is an ideal site for regional therapy with chemicals or biologicals, and indeed topical therapy with chemotherapeutic agents or BCG has been the mainstay of therapy for bladder papillomas. It may be that antisense compounds mirroring the genetic sequence of certain key cancer-causing genes will be useful therapeutic agents here. Photodynamic therapy—a new way of sensitizing cells to visible light—has potential usefulness for thin layers of premalignant epithelial cells covering the surface of the mouth or esophagus.

For early diagnosis and detection, NCI is moving forward to establish a multicenter trials network for diagnostic imaging. This network will incorporate centers of excellence in imaging research and practice throughout the country and will collaborate with the imaging device industry and with third-party payers to accomplish the rigorous clinical assessment of technological innovation. We expect that anatomic sites affected by tobacco will receive significant emphasis.

To meet these challenges, we must have a clinical research base that can bring the best of

our emerging knowledge about tobacco-related cancers along with the best ideas, best technologies, and best people to the problems of prevention, detection, diagnosis, and treatment of these diseases. It is dismaying that only about 2% of adult cancer patients participate in clinical trials. The reasons for this low participation are complex including issues related to our society's health care system as well as issues related to the perception of the public regarding clinical research. The NCI would like to see all eligible cancer patients participating in clinical trials. Accomplishing this very ambitious goal will involve utilizing considerable resources to lower the barriers to participation. This will include "user-friendly" access to information about clinical trials as well as additional financial support for clinical trials. The resources of the PHTF would enable these barriers to be lowered on a time-scale that would otherwise be impossible.

3. Prevention of tobacco-related cancers for 45-50 million former smokers

About half of all living Americans who ever smoked have quit. Yet premature deaths from smoking will continue for many years to come, even if all smokers were to quit today. Heavy smokers retain some elevated risk for lung cancer when compared to never-smokers, even after 20 years of cessation. More than 50% of lung cancers diagnosed in the late 1990's occur in ex-smokers. Thus, the 45 to 50 million Americans who are former smokers are a population that could benefit greatly from chemoprevention research. They already have taken a major step toward improved health, but require new medical options to gain full advantage from this step.

Previous clinical studies have defined high-risk populations that should facilitate future detection and prevention trials. For example, lung cancer patients with completely resected stage I disease are at particularly high risk for second primary lung cancers. To a lesser degree, the 45-50 million ex-smokers represent a pool of high-risk individuals. The large population of former smokers in the Department of Defense, Veterans Administration and managed care systems makes access to individuals for clinical trials in prevention possible.

Promising preventative interventions (e.g., vitamin A analogs, selenium, non-steroidals and specific growth pathway inhibitors) are ready for testing. Prevention studies using aerosolized delivery of new targeted therapies including gene therapies, antisense therapeutics, and targeted small molecules will also need to be conducted. Key to these studies will be the identification and validation of intermediate biomarkers that will be used to define the activity of new preventative interventions. The research that underlies an undertaking of this magnitude is significant. The trials themselves will be massive and expensive to conduct. The PHTF offers the opportunity to move these efforts onto the fast track. Given current funding limitations, this would not be possible otherwise.

4. Development of preclinical models for tobacco-related cancers

For clinical trials to have a good chance of success, the interventions being tested in them should have to pass stringent tests in the laboratory that suggest they might work. For these laboratory tests to be valid predictors of what will happen in people, the laboratory models must be accurate mimics of human disease. For cancer this means that laboratory cancers should bear fairly close resemblance to human cancer in their molecular characteristics. The failure of some large clinical trials is attributable, in part, to the lack of predictive laboratory models for human cancer. Most current animal models have not proven of much utility in tobacco and smoking investigations, despite studies confirming the development of cancer in

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beagles chronically subjected to tobacco smoke. The use of dogs as routine models in cancer prevention studies (other than toxicity studies) has been very limited because of availability, and costs associated with purchase and maintenance. More recently, the exposure of certain rodents to specific tobacco smoke ingredients has resulted in lung cancer development. New animal models including an orthotopic lung cancer model which metastasizes in a pattern similar to that in humans may provide the means to study new preventative, diagnostic, and therapeutic approaches to lung cancer.

Biological advances have changed the prospects for developing such models, and it is now possible to engineer cells or even whole animals to have certain genetic properties that are desirable in cancer models. Much more work is needed to develop and refine preclinical models of the major tobacco-related cancers, so that clinical work in both prevention and treatment can proceed with a higher probability of success. The PHTF would allow for increased investment in the development of improved animal models for tobacco-related carcinogenesis including intermediate biomarkers for assessment of exposure to tobacco and the biological effects of such exposure with validation these models in parallel studies in animals and humans. It is also possible to use non-mammalian organisms to study the basis of tobacco-related carcinogenesis. The NCI would like to sponsor studies to determine whether metabolic pathways in "simple organisms" (e.g., *C. elegans*, *Drosophila*, *Xenopus*, Zebrafish, yeast, etc.) that are analogous to those involved in human cell transformation can be exploited in drug discovery for tobacco-related cancers. It may also be possible to study chemopreventative interventions at much higher efficiency once these models are developed. However, the research required to reach this goal is considerable. Without the resources provided by the PHTF, this important research would be delayed significantly, if in fact it could be done at all.

5. Exploration of cancer susceptibility and gene-tobacco interactions

It has become increasingly clear that a person's genetic makeup influences susceptibility to environmental agents such as tobacco smoke. Everyone knows individuals who have smoked for long periods of time without contracting cancer. What distinguishes these individuals from those who with the same tobacco exposure get lung cancer and die from the disease? The answer to this question resides in the understanding that cancer susceptibility is not a simple function of genes or environment but rather a function of the complex interplay of genes and environment. We need to identify the genes that influence susceptibility to tobacco and to understand how these genes function to modulate tobacco's carcinogenic potential. The identification of these genes will enable us to predict who is at the highest risk for cancer development allowing for better counseling, prognosis, and detection. This identification will also open research opportunities to develop therapies to counteract the high susceptibility to cancer development. The identification of these genes would only be possible within the foreseeable future through the increased investment afforded by the PHTF. The project is extremely costly involving years of case-control studies involving thousands if not tens of thousands of individuals. This project would entail the collection and maintenance of biological tissues and fluids from large population groups, the measurement of environmental exposure (e.g., through measurement of nicotine metabolites), development and use of a detailed questionnaire involving environment and behavior, and an informatics system capable of storing and analyzing the massive amounts of data generated in such a study.

Research enabled by the PHTF that is aimed at understanding the genetic predisposition to

tobacco-related cancers will include the development and expansion of biorepositories to provide access (with appropriate consent) to such materials as new hypotheses emerge. Such biorepositories also facilitate the identification of new molecular markers for cancer and precancerous lesions. Such markers are essential for the development of new early detection of tobacco-related cancers. Once such markers are found, they will require extensive clinical trials to assess their prospective value.

A significant fraction of what we know about carcinogenesis has its origins in studies of individuals with higher-than-average risk of cancer. The studies of rare hereditary disorders such as retinoblastoma and Li-Fraumeni syndrome have led to insights into cancers that are much less rare than these inherited diseases. The detailed examination of high risk individuals (i.e., individuals with current or past exposures to high levels of tobacco) will likely extend this paradigm. In fact, it seems very likely that benefits will accrue to non-smokers from the PHTF-sponsored research involving past or current smokers. This putative benefit is altogether fitting given that the entire society bears the cost of tobacco-related disease.

6. Improved early detection and diagnosis of tobacco-related cancers

Tobacco-related cancers present attractive opportunities for the development of much more accurate methods for earlier detection and better diagnosis. The population at risk is largely defined (i.e., current and past smokers), and many classes of tobacco-related cancers occur in anatomical locations accessible to biopsy or the obtaining of biological specimens (head and neck, esophagus, bladder) or radiological images (lung). It is a reasonable expectation that more sensitive diagnostic techniques will increase cure rates, since early cancers are, in general, more curable than advanced ones. Molecular techniques can now pinpoint cancer-causing mutations in the DNA of cells that appear in cells or cell debris from the mouth, aerodigestive tract, urine. More sensitive digital imaging and image-processing techniques are in development that should allow the detection of much smaller tumors in the lung, a notoriously difficult site for early detection. Emerging technologies related to high-throughput, cost-effective, comprehensive molecular analysis will soon allow a complete molecular profile of cancer cells and precancerous lesions. The translation of these emerging technologies to applications that benefit large number of patients is a daunting but necessary task. The PHTF could enable this to occur much more rapidly than would otherwise be possible.

Through the PHTF, the NCI could begin to fund testbeds for innovations in diagnosis emerging from either academia or industry (for example, new diagnostic devices based on molecular biology or imaging technology). Initial funding would probably involve the 55 existing NCI-designated Cancer Centers. These settings facilitate multidisciplinary collaboration between the sources of technological innovation and the scientists and physicians who can provide the necessary biomedical perspectives, tissue resources, and clinical setting for actual testing. Prototype devices could be subjected to pilot testing in these settings; these pilot tests may result in decisions to continue up the development ladder or may indicate the need for further refinement in the laboratory before broader testing. The fostering of collaborations between imaging scientists and investigators in other areas of biology and medicine will serve to hasten the development of non-invasive methods of tumor characterization important to foster improvements in diagnosis, prognosis, and treatment of tobacco-related cancers. The scale of this project requires resources such as those provided by the PHTF.

7. Improved National surveillance of tobacco-related cancers

The NCI desires to enhance our ability to gather more extensive and more intensive data on the burden of tobacco-related cancers throughout society, in order more readily to develop and test hypotheses about trends in the incidence and outcome of these cancers as patterns of tobacco usage change and as effective interventions are introduced on a large scale. The PHTF will enable this desire to become a reality.

The effects of changes in utilization of tobacco products by the American people, together with the results of implementing effective preventive or early diagnosis strategies nationally, when these become available, will be difficult to discern without adequately sensitive surveillance programs. NCI would like to reexamine its important databases such as the Surveillance Epidemiology and End-Results Reporting (SEER), which tracks the impact of cancer on the general population. The SEER database has proven to be of great utility to the scientific community but the SEER database contains only about 13% of the US population and representation of racial and ethnic groups within the database vary widely. There are also limitations to the depth of data collection and entry that is possible with the current level of funding. The PHTF would enable a significant enhancement of this database both quantitatively and qualitatively. We want to make sure that, to the maximum extent feasible, the SEER database not only tracks changes in cancer incidence and survival accurately, but also contains enough of the right kind of information to enable the generation of hypotheses about the basis for any observed changes in trends over time. New initiatives will be developed to expand surveillance research to allow more complete collection of information on risk factors, including exposure to tobacco. Emphasis on underserved or special populations at high risk (e.g. age, race/ethnicity) will be a key component of the program.

Establishing new linkages between databases containing different kinds of health-related information on populations is a very powerful tool for certain kinds of analyses. Advances in information technology will enable linkages like these to be established much more easily than in the past and, in time, will facilitate the creation of databases through electronic transfer of information from electronic source documents. The ease of long-distance communication made possible by the World Wide Web and other features of the Internet will create opportunities for collaboration and data sharing across national borders and oceans that have never before been a practical reality.

8. Improved communication about tobacco-related cancers and interventions

The power of computer-based communications and the capabilities of the World Wide Web will make possible new levels of cooperation in research on patients and populations. With funding from the PHTF, the NCI would embark on the implementation of an ambitious series of information networks to serve a needs of cancer research nationwide. Slow and cumbersome paper-based systems of data collection for multicenter studies will give way to electronic communication, facilitated by enhanced links between sources of data at points of care delivery (hospitals, offices, clinics) and the research database on which analysis of results is based. In collaboration with other Federal agencies, and with the participation of many external scientists and clinicians, NCI will modernize information links with its investigators, in a manner that will be compatible with standards set by the International Committee on Harmonization for North America, Europe, and Japan. We would also revise our criteria and standards for reporting adverse drug reactions and treatment-related toxicity. The results will be a set of common reporting requirements and terminological standards that will greatly

Increase speed and efficiency in the reporting of clinical trials both to sponsors and to regulatory agencies. NCI's long-range plans are in early stages of formulation now, but will call for the development of informatics systems and architectures that assist clinicians participating in trials with many aspects of the data collection and treatment process; the aim here is to reduce or eliminate barriers to participation in trials and to reduce the gap, wherever it exists, between the requirements of routine care and care on clinical research studies.

The potential of the computer as an instructional tool is just beginning to be tapped. Instructional modules on computer tailored for individual needs (i.e., semi-personalized courses) are likely to be much more effective than currently standard techniques for teaching people about concepts like the risk of getting a disease given a certain genetic predisposition, lifestyle characteristic, or environmental exposure. In the form of kiosks in public places like libraries or malls, computers can inform people about research results or studies of possible interest and relevance to them. NCI is already exploring this possibility in collaboration with the State of Maryland as a pilot study. The PHTF would enable this pilot to fly nationwide. With the active collaboration of several patient advocate groups, NCI beginning an ambitious effort to create a "patient-friendly" database, containing information on cancer and on clinical research protocols in nontechnical language. This will provide for enhancement of NCI's current large-scale efforts to provide the general public with access to up-to-date information about new research results, available clinical trials in diagnosis, treatment, and prevention, and contact points for additional information. This is a very large and ambitious project. The nationwide dissemination of this information system would not be possible without significant funds outside the current NCI appropriation. Without an external source of funding like the PHTF, it will be years before substantial headway can be made on this project. It is believed that this way of publicly disseminating information via computer will be of particular appeal to the current generation of adolescents who are as a group more "computer-literate" than previous generations. Public libraries also provide access to underserved populations.

IV. NATIONAL HEART, LUNG AND BLOOD INSTITUTE (NHLBI)

The mission of the NHLBI is to provide leadership for a national program in diseases of the heart, blood vessels, lung, and blood. This year, about 430,000 Americans will die of smoking-related illnesses. More than 250,000 of these deaths are attributable to heart disease, stroke, or chronic obstructive pulmonary disease, all of which fall within the mandate of the National Heart, Lung, and Blood Institute (NHLBI), NIH. These diseases are worldwide problems that are rapidly overtaking mankind's traditional scourges—infections and malnutrition—as contributors to the global burden of disease.

Beginning with the famous Framingham Heart Study, initiated in 1948 by the NHLBI, research has systematically documented that smokers are particularly susceptible to developing heart attacks, strokes, and chronic lung diseases; that heavy smokers have a greater risk than light smokers; that smokers in their late teens and early twenties already show evidence of clogged arteries and symptoms of reduced lung function; that, among persons with high blood pressure or high cholesterol, smoking seriously magnifies the already increased risk of heart attack or stroke; and that quitting smoking at any age greatly reduces the likelihood that these catastrophic events will occur. These findings have formed the basis for educational campaigns to raise awareness among the public and health-care professionals that abstinence from smoking "makes the heart grow stronger" and to promote screening to identify smokers with early lung abnormalities.

These research efforts have been impressive, but much more needs to be done. Additional resources, such as those envisioned in the PHTF, would accelerate progress toward eliminating the burden of this public health threat. Research opportunities abound. For instance, our knowledge of the connection between smoking and disease has been based on probabilities calculated from observations of large populations. Thus, a given smoker can be advised that this habit increases the risk of developing an illness, but we cannot predict with any certainty whether he or she can expect to die of a heart attack, a stroke, chronic lung disease, or lung cancer or live to age 100 in the pink of health. Science has now reached the point where we may be able to discover the genes that govern individual susceptibility to the ill effects of smoking. This information will not only permit a personalized approach to preventive health counseling, but also open up new possibilities for treatment and cure based on a better understanding of how and why smoking-related diseases develop.

A. Tobacco-Related Research of NHLBI

Worldwide, tobacco smoking causes millions of deaths each year, many of them from cardiovascular diseases (coronary heart disease, peripheral vascular disease, stroke) and chronic lung diseases (chronic bronchitis, emphysema). Thus, research on the adverse health effects of cigarette smoking, the health benefits of cessation, and the impact of environmental tobacco smoke (passive smoking) on lung function impairment, atherosclerosis, hemostasis, and thrombosis in both adults and children is of high priority to the NIH.

In FY96, NHLBI expenditures for research related to smoking and health totaled ~\$26M. This figure included the Lung Health Study, a large-scale clinical trial of smoking cessation and pharmacologic therapy in smokers at high risk of developing chronic obstructive pulmonary disease; studies of smoking cessation strategies targeting men and women of a variety of ages, racial/ethnic backgrounds, and socioeconomic strata; research on prevention

of active and passive smoking in children; basic studies of the mechanisms by which smoking causes tissue damage; and epidemiologic observations of smoking as a risk factor for cardiovascular and lung diseases. The importance of tobacco avoidance is a key message of the Institute's educational programs, such as the National High Blood Pressure Education Program and the National Cholesterol Education Program. Because of the nature of the NHLBI's mission and the huge contribution of tobacco to diseases of the heart, lungs, and blood, much of the NHLBI's efforts are focused on tobacco-related diseases.

Innovative and exciting new directions in genetics and genetic epidemiology now have the potential to provide new information about the underlying biological mechanisms of injury caused by tobacco smoke and to identify the genes involved and determine how they work. Some of the multiple opportunities for smoking-related research and their potential impact on cardiovascular and pulmonary diseases are summarized below.

B. NHLBI Plans for Research on Tobacco-Related Diseases

1. Genetics of susceptibility to smoking induced target-organ damage

Individuals with identical risk factor profiles vary considerably with respect to the course of a disease and the extent of damage it causes to target organs, such as the lungs and the cardiovascular system. For example, when people smoke or are exposed to tobacco smoke, some are susceptible to developing chronic lung or cardiovascular disease, while others seem to be protected. Evidence is emerging that there is a genetic basis for this variability in susceptibility to target organ damage. Identification of susceptibility/protection genes would provide innovative approaches for the development of new treatment and prevention strategies. Mapping, isolating, and characterizing these genes is complicated because multiple genetic and environmental factors interact in complex ways. However, information from the Human Genome Project, advances in analytical and statistical approaches, and new study designs now make it feasible to explore this promising research opportunity. The magnitude of this project would necessitate resources like those from the PHTF.

2. Families at risk of cardiovascular disease

Data suggest that a significant proportion of families afflicted by cardiovascular diseases may have cigarette smoking as their only identifiable risk factor. The existence of such families points to a genetic contribution to susceptibility to the specific effects of smoking on the cardiovascular system, but these genetic factors have not been well defined. This could occur via the PHTF. Targeted family-based studies of cardiovascular disease and its risk factors in both active and passive smokers would facilitate identification of genes and, thereby, enhance understanding of the mechanisms by which smoking increases risk for cardiovascular disease. Once identified, wide-scale screening for such genes in active smokers could enable identification of those most susceptible as candidates for intensive cessation efforts.

3. Genes that confer protection from smoking-induced diseases

Advances in molecular genetics make it possible not only to look for genetic factors that cause cardiovascular and lung diseases, but also to discern genetic factors that prevent or retard their progression. Just as susceptibility genes may predispose many to disease, "protective" genes may confer resistance. With support from the PHTF, NHLBI would seek to identify specific "protective" markers that may improve understanding of the etiology of these

common diseases and also assist in the development of new drugs or other therapies to treat them.

4. Identification of exposures that interact with smoking to induce disease

It has been reported that co-exposures, either biological or nonbiological, may interact with genetic factors to increase an individual's adverse response to tobacco smoke exposure. Co-exposures may trigger strong immune responses in certain individuals, thereby increasing susceptibility to smoke-induced damage. With currently available techniques in cellular and molecular biology, it is now possible to study mechanisms by which these co-exposures may contribute to the development of cardiovascular and pulmonary diseases. The PHTF could significantly speed this process.

5. Components of tobacco smoke that cause tissue damage

Nicotine stimulates the sympathetic nervous system and causes adrenal release of catecholamines, which increase heart rate, blood pressure, stroke volume, and cardiac output. Increased epinephrine and norepinephrine levels in the circulation affect various hematologic, metabolic, and endocrinologic processes and influence the development of atherosclerosis and its complications. In normal individuals, the increased work of the heart results in increased coronary blood flow. However, patients with compromised coronary and peripheral circulation may develop angina, heart attack, or sudden cardiac death. Other components of cigarette smoke (e.g., nitrogen oxides, carbon disulfide, cadmium, and possibly tar) may also contribute to cardiovascular pathology and merit detailed study. The comprehensive study of the many tobacco components and the interaction of each with tissue would require the resources of the PHTF.

6. Innovative investigations of the role of inflammation in smoking-related illness

Inflammation has recently been recognized as a key promoter of the atherogenic process, and smoking is known to be strongly related to inflammatory processes in the lung. The systemic effects of inflammation, such as elevated circulating levels of inflammatory mediators or enhanced thrombogenicity, have not been examined in relation to risk of atherosclerosis and endothelial dysfunction. These effects could readily be studied in smokers and persons exposed to environmental tobacco smoke, as well as in persons in smoking cessation programs whose exposure may have wide variations over time. Biological measures of direct smoke exposure and metabolism, coupled with serum markers of inflammation, should be correlated with noninvasive measures of atherosclerosis and endothelial function in population-based samples of persons free of known cardiovascular and pulmonary disease. Such large-scale studies could provide critical insights into the mechanisms by which smoking induces atherosclerosis and chronic lung disease but would require the resources of the PHTF.

7. Research on the interaction between smoking and therapeutic drugs

Cigarette smoking has been reported to interfere with the pharmacodynamic and pharmacokinetic profiles of certain drugs—including those utilized in the treatment of chronic conditions such as hypertension, angina, arrhythmia, dyslipidemia, asthma, and diabetes—thereby compromising drug efficacy. Possible mechanisms for these reported

cigarette smoking-drug interactions have been proposed, but little is known about their effects on patient outcomes or their underlying pharmacologic mechanisms. Both questions could be addressed with support from the PHTF.

8. Exploration of strategies to reverse tissue damage in emphysema

Although the lung tissue destruction that characterizes emphysema has always been thought of as irreversible, some evidence to the contrary has recently emerged. An interesting report indicated that in small animal models in which elastase was administered to produce emphysema-like changes in the lungs (larger airspaces and decreased number of alveoli), treatment with retinoic acid returned the lung alveoli to normal size and number. While these data suggest that emphysema may be reversible, this work must be substantiated in other animal models of smoking-induced emphysema before research in humans can even be contemplated. All animal model studies are costly and the validation in humans of findings from animals is even more costly. The PHTF could aid in these studies.

9. Surveillance of trends in smoking-related morbidity and mortality

Given the numerous serious chronic diseases related to smoking and the substantial shifts in smoking patterns (decreases in older and middle-aged men, increases in young women) that have occurred in recent decades, trends in morbidity and mortality can be expected to change dramatically in the next several years. Accurate information will be critical to guide future public health and research efforts in this area. National vital statistics are not sufficient for this purpose, because ascertainment of cause of death from death certificate data is problematic and mortality information fails to capture the majority of suffering and health care costs related to these illnesses. A broadly representative, community-based system for ascertaining and verifying incidence, prevalence, hospitalizations, and disability from the common serious illness caused by smoking is required to monitor future morbidity trends and focus efforts in research and prevention. As with any surveillance system, this one would require significant support not only for data collection but for the informatics backbone that would be required for storage and analysis of the data. Such a system could be possible with resources from the PHTF.

10. New strategies to prevent smoking initiation in the young

Once initiated, smoking behavior is costly, and research consistently demonstrates that even effort-intensive approaches to smoking cessation often achieve relatively minor results. Because the majority of smokers (82 percent) began smoking daily before age 18 and 3,000 young persons take up the habit every day, tobacco prevention activities focused on school-age children and adolescents are an urgent priority. Prospective epidemiological studies are needed to understand the risk factors leading to the initiation of smoking behavior and patterns of tobacco use. Risk factors for smoking behavior—including accessibility, availability, attitudes, price, socio-cultural and religious beliefs, psychosocial variables, peer pressure, age, gender, minority status, parental smoking, and role models—need to be identified and classified. Research supported by resources from the PHTF should compare the effect of socioeconomic status on smoking behavior in various racial/ethnic groups in an effort to increase understanding of population needs and enable the design of cost-effective, culturally sensitive interventions.

11. Investigations of the health prognosis of ex-smokers

It is generally believed that the risk of smoking-related lung diseases, including cancer, in ex-smokers returns to the level of never-smokers only after 10-15 years of abstinence. A better understanding of the rates at which ex-smokers continue to lose lung function and/or regain their lost function is important to assess quality of life and disease susceptibility. The PHTF could enable these important parameters to be assessed. Specifically, studies are needed to delineate the time course of loss/recovery of lung function and the potential for developing lung disease among various populations of ex-smokers, with the ultimate goal of developing interventions to recover/repair/remodel tissue damage caused by smoking.

12. Improved understanding of the relationship between smoking and body weight

Weight gain is often an unfortunate consequence of smoking cessation, and overweight is, itself, a risk factor for cardiovascular disease. Research is needed to determine the mechanisms underlying the weight-suppressing effect of smoking and the weight-increasing effect of smoking cessation, so that interventions to counter them can be developed. This represents a question that may be extremely relevant to smoking cessation in adolescents and is the kind of large study that would benefit from PHTF resources.

13. Maternal smoking and fetal/child health

Maternal smoking adversely affects fetal growth, but the reasons for this phenomenon are not clear. Recent studies have suggested that in utero tobacco exposure increases the incidence of a specific cluster of congenital heart defects, cleft palate and other craniofacial abnormalities, and abnormal neurological development and also results in abnormal lung growth and function after birth. Infants and children who live in households with smokers experience increased rates of ear infections, sinus infections, upper respiratory infections, reactive airway disease, and pneumonia, and as a result are hospitalized more frequently. The incidence of these health burdens increases with the number of adults in the household who smoke. More research is needed to explore the effects of exposure to smoking on the maternal-fetal unit, childhood physical and mental health, and future health problems (e.g., increased risk of cancer), so that effective preventive measures can be developed. The PHTF could enable this research.

14. Tobacco exposure and asthma exacerbations

Tobacco smoke is a major precipitator of asthma symptoms in children and adults. Exposure by adults with asthma to environmental tobacco smoke is associated with decreased levels of pulmonary function, increased requirements for medication, and more frequent absences from work. Research into the mechanisms whereby smoking increases bronchoconstriction and mucus secretions in individuals with asthma will provide important insights into the progression of asthma severity and could greatly benefit from the resources of the PHTF.

15. Smoking, estrogen, and deep vein thrombosis

Deep vein thrombosis and pulmonary embolism have been reported in young women who smoke and use estrogen-containing contraceptives. Emerging data suggest that women who smoke and use postmenopausal hormone replacement therapy may also have suffer similar complications. Hormone replacement therapy is being widely recommended not only for

symptomatic relief of perimenopausal symptoms, but also for its potential benefits in reducing the risk of coronary heart disease and preventing osteoporosis. More research is needed to unravel the complex relationship between cigarettes, estrogen, and deep vein thrombosis, as well as to develop methods to identify women, particularly cigarette smokers, who are at high risk of developing deep vein thrombosis when using natural or synthetic estrogens for hormone replacement or contraception. The PHTF could enable this research to be performed.

16. Demonstration research on smoking prevention in the young

Demonstration research projects should carefully design and evaluate comprehensive interventions combining smoking prevention education at school, in pediatricians' offices, in dentists' offices, and at home. To move resulting research successes into practice, assessment of the degree of implementation of proven programs is needed, followed by research examining the effectiveness of approaches to disseminating the programs. This type of research is costly and time-consuming. The PHTF could facilitate its completion.

17. Interventions for populations of low socioeconomic status

Nationwide public health efforts at disease prevention have enjoyed much success, but their benefits have not been fully realized across all segments of society. Despite targeted attempts, participation in prevention programs by persons of low socioeconomic status continues to lag. In addition, cultural characteristics, economic status, language differences, inaccessibility of cessation programs, and targeted promotional activities by tobacco companies have placed the more disadvantaged members of our population at higher risk. Effective, culturally sensitive programs of prevention need to be developed and carefully evaluated for all populations at risk. Individuals of lower socioeconomic status appear to have been disproportionately harmed by tobacco. The PHTF could enable research aimed at remedying this situation.

IV. NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT (NICHD)

The NICHD conducts and supports laboratory, clinical and epidemiological research on the reproductive, neurobiologic, developmental, social and behavioral processes that determine and maintain the health of children, adults, families and populations. With regard to the proposed tobacco settlement, the NICHD has a major role in research related to discouraging children and adolescents from starting to use tobacco and in helping these groups, as well as pregnant women, to stop smoking. In addition, the NICHD has a role in research on the tobacco-related medical conditions of low birth weight and sudden infant death syndrome (SIDS).

A. NICHD Research to Discourage Starting and to Assist Quitting Tobacco Use

1. Basic studies of behavioral development and change

Smokers begin smoking early with 16% of adult smokers having begun before age 12; 37% before age 14, 62% before age 16, and 89% before age 18. Given these statistics, it is not surprising that researchers acknowledge that programs to prevent the onset of smoking or other risky behaviors should start *before* adolescence, when children are still in their *middle childhood* years (between kindergarten through six grade). In FY96, NICHD funded studies in this area totaling ~\$5.5M.

The NICHD leads efforts to better understand the social, emotional, and intellectual patterns of growth and rapid change that characterize the middle childhood years, and to understand how children's changing relationship with their parents and widening exposure to their communities and a variety of peers influence their chance for adopting unhealthy behaviors. NICHD-supported researchers are also trying to develop predictive measures of risk in this younger population, and have already identified four "protective" factors that can be targeted when developing programs to prevent the onset of smoking. The NICHD has led another effort to identify developmental measures that are appropriate for minority populations. Other studies, involving ethnically diverse youth starting in middle childhood, are examining the development of risk perceptions.

2. Surveillance

Any successful smoking prevention program must be developed with a firm understanding of how smoking and related risk behaviors, as well as contributing risk-factors, are distributed in various populations and change over time. Surveillance and epidemiologic studies also help researchers understand the link between smoking and a range of adverse health outcomes. These areas of research were supported by NICHD in FY96 at a level of ~\$2.8M.

The NICHD supports a range of epidemiologic studies targeting the impact of maternal smoking and environmental exposure to smoke on pregnancy outcomes and on child development. In particular, a large study involving 8,000 women in prenatal care is examining tobacco smoke as a risk factor for premature rupture of membranes. Other studies concern spontaneous abortion and intrauterine growth retardation in women who smoke, as well as the health and development of children with prenatal exposure.

The NICHD has supported the Add Health Study, an unprecedented survey documenting the health and health behaviors of adolescents, as well as the factors that contribute to these.

outcomes (which include smoking). Another study, using survey data on youth and their families, is helping to distinguish between the genetic and environmental influences that lead children to adopt high risk behaviors, including smoking.

3. Public Health and Community-Based Studies

The NICHD supports a range of community-based prevention and intervention studies to prevent youth from starting to smoke or adopting other high risk behaviors. These studies build on the surveillance and basic behavioral research mentioned above and in FY96 totaled ~\$1M.

NICHD intramural researchers have designed and implemented a study to test the efficacy of a school-based program in preventing problem behaviors. This study, which involves 3,000 middle school students in a three-year prevention program, targets the common factors that lead to smoking, as well as other risk behaviors. It has a unique education component to help parents increase the monitoring, involvement, and support of their middle-school child.

Another NICHD-supported community-based study brings researchers and community organizations together to develop, implement, and evaluate interventions, targeted to minority youth, to help them develop the skills necessary to avert and avoid risky behaviors, ranging from substance abuse (which often includes tobacco use) to other high risk behaviors.

B. NICHD Plans for Expansions of Tobacco-Related Prevention Research

1. Smoking prevention programs targeting middle childhood

Based on the observation that the longer health risk behaviors can be delayed, the less likely they are to start, the NICHD could expand its middle childhood initiative with resources from the PHTF. Starting with a conference addressing cigarette smoking and middle childhood, already scheduled for September 1997 with multiple Institutes participating, researchers will develop a multidisciplinary research agenda outlining the next generation of studies to help prevent children from starting to smoke. To conduct this research, four to six health risk prevention research centers would be established, combining the talents of researchers from the biological, behavioral, and social sciences. The centers would identify which of the "protective" factors identified to date are most important and amenable to the development of interventions, and employ longitudinal studies to test the effectiveness of different prevention approaches, as children make the difficult transition from elementary to middle- and high-school. The PHTF could enable this important research to go forward.

2. Helping adolescents to stop smoking

To date, researchers have focused on how to prevent teenagers from starting to smoke and helping adults learn how to stop smoking; few researchers have targeted the important issue of how to help adolescents stop smoking. With PHTF resources, the NICHD plans to expand its multidisciplinary research to better understand how many developmental factors—ranging from hormonal to other physical, cognitive and social changes—affect the ability of teens to stop smoking, and to develop and test interventions to do so. The Add Health study could also be extended to collect a new round of longitudinal follow-up data to see how teen behaviors actually change over time, integrating social, psychological, and biological perspectives. In addition, several of the intervention studies targeting minority youth and the

changing of high-risk behavior could be replicated in new sites and contain a smoking-cessation component. The NICHD intramural study to prevent problem behaviors in schools could be expanded to new sites with increased emphasis on reducing the onset of smoking by young adolescents.

3. Helping pregnant women to stop smoking

Given that smoking is significantly linked to adverse birth outcomes, effective behavioral modification programs must be developed for pregnant women. The NICHD has developed one approach, "Baby and Me, Smoke-Free," but has never had funds to test it. In addition, marketing approval has not been sought to use the "nicotine patch" during pregnancy. Priority must be given to completing pharmacokinetic studies, safety evaluations, and clinical trials to allow pregnant women to have access to this important means to stop smoking.

C. Research of NICHD on Tobacco-Related Conditions

The NICHD supports extensive research on pregnancy and maternal health, fetal growth and maturation, labor and delivery and infant well-being. These studies include elucidation of the normal and abnormal factors that influence the course and outcome of pregnancy, such as maternal physiology and environmental variables, and those events, conditions and treatments occurring during pregnancy which contribute to a low-birth-weight (LBW) infant or other adverse outcome. Basic and clinical studies on infant health include the etiology, pathophysiology, therapy and follow-up of conditions and syndromes affecting infants, including LBW and SIDS, key factors in infant mortality. Environmental factors are important, with maternal smoking alone accounting for as much as one-third of LBW incidence. Of all the things we know, stopping smoking during pregnancy would have the greatest effect on reducing LBW. Independently, prenatal and postnatal exposure to smoke each dramatically increases an infant's risk of SIDS, approximately threefold and twofold, respectively. Therefore, an understanding of the mechanisms by which this increased incidence of LBW and SIDS occurs would contribute to a major reduction in infant mortality and morbidity.

1. Low Birth Weight Infants

The NICHD has a substantial portfolio of research on LBW and preterm delivery totaling ~\$62M in FY96. Ongoing studies demonstrate that bacterial vaginosis (BV), a common vaginal condition, significantly increases a woman's risk of premature delivery of a LBW infant and that, in addition to BV, smoking increases the risk of preterm delivery by 40%. Other research attempts to identify new approaches to achieving fetal maturation when preterm birth is likely.

NICHD supports networks of Maternal Fetal Medicine Units (MFMUs) and Neonatal Intensive Care Units (NICUs), to conduct multicenter randomized clinical trials and other prospective clinical studies in obstetrics and neonatology, especially targeted to both the treatment and prevention of LBW. The multidisciplinary Perinatal Research Emphasis Centers (PERCs) fund basic, preclinical and clinical research addressing the complex problems of pregnancy and perinatology, including intrauterine growth retardation, fetal hypoxia, fetal maturation and initiation of preterm labor.

2. Sudden Infant Death Syndrome

Current research includes studies to determine the underlying mechanism of SIDS and its probable cause(s), and to develop preventive approaches. SIDS research totaled ~\$11.5M in FY96. Emphasis is placed on research concerning the identification of infants at risk of becoming SIDS victims. This includes both basic and clinical studies of the neurophysiologic, cardiorespiratory, metabolic, immunologic, genetic, pathologic, environmental and infectious disease aspects of the syndrome. Studies also try to determine the relationship between high-risk pregnancy, high-risk infancy, and SIDS.

D. NICHD Plans for Expansions of Research on Tobacco-Related Conditions

1. Low Birth Weight Infants

With the PHTF, research could be conducted including the role of tobacco as a maternal risk factor for LBW and preterm delivery. Increased investment via the PHTF in the PERCs, NICUs and MFMUs could greatly enhance basic knowledge about the etiology of LBW, its prevention and its treatment. For example, additional funds would accelerate accrual for a clinical trial to determine if screening for and treating BV in the first trimester of pregnancy is safe and effective. Additional support for the intramural Perinatology Branch would expand studies on the precursors of and disorders associated with infant mortality. Additional funds from PHTF would expand the NIH-DC Infant Mortality Initiative, a trans-NIH study of the determinants of the high infant mortality rate in the District of Columbia.

2. Sudden Infant Death Syndrome

In addition to supplementing the ongoing basic and intervention studies related to SIDS, specific initiatives are proposed using PHTF resources. Some scientists believe that smoking is part of the causal pathway to SIDS, possibly through intrauterine hypoxia. In trying to delineate the mechanisms for increased risk of SIDS, it is important to differentiate between direct biologic actions of components of cigarette smoking on the maternal-fetal unit or the infant, and the behavioral factors associated with cigarette smoking. Some fruitful areas of research would include studies to: differentiate between direct effects of smoking on SIDS risk versus factors like reduced nutrition, maternal depression and increased susceptibility to infection associated with cigarette smoking; develop animal models on how smoking could impair autonomic nervous system development and function in early infancy, and lead to sudden death; elucidate the sleep, cardiorespiratory and immune system physiology of infants exposed to large doses of cigarette smoke pre- and postnatally; and develop more effective interventions to reduce cigarette smoking in the fetal and infant environment.

VI. NATIONAL INSTITUTE OF DENTAL RESEARCH (NIDR)

The mission of the National Institute of Dental Research (NIDR) is to promote the general health of the American people by improving their oral, dental and craniofacial health. Through nurturing fundamental research and the development of researchers, the NIDR aims to promote health, to prevent diseases and conditions, and to develop new diagnostics and therapeutics. Knowledge acquisition through science and effective and efficient science transfer are the means used to contribute to improved quality of health. The National Institute of Dental Research (NIDR) spent approximately one-fourth of its \$187 million appropriation in FY96 on diseases related to tobacco including craniofacial, oral and dental disease research. The three primary program areas that comprise NIDR's tobacco-related research include oral, pharyngeal and nasopharyngeal cancer, periodontal diseases and craniofacial birth defects.

A. Tobacco's Impact on Oral Health

Tobacco product uses (e.g., smokeless chewing tobacco and snuff, and cigar, pipe and cigarette smoking) are the number one risk factor responsible for oral, pharyngeal and nasopharyngeal cancers; that claim over 8,000 lives each year. Another 4,250 lives are lost to cancer of the larynx. It is estimated that 82% of laryngeal cancers are due to cigarette smoking. The incidence of oral cancer among smokers ranges from 2- to 18-times that among nonsmokers. At least 28 tumorigenic agents have been isolated and identified in smokeless tobacco products, nicotine being just one of these.

Internationally, the incidence of oral cancer is increasing. Throughout the world, malignant neoplasms of the mouth and pharynx rate as the fifth most common cancer in men and the seventh in women. Excluding facial skin, the majority of malignant neoplasms (over 80%) in the oral and pharyngeal region are squamous cell carcinomas of the oral and pharyngeal mucosa, tongue and lips. In industrialized countries, men are affected twice as often as women; and African American males are affected at twice the rate of Caucasian males. In the United States, one American dies every hour of oral cancer. There are approximately 42,000 new cases of oral, pharyngeal, nasopharyngeal and laryngeal cancer reported each year. The prognosis after 5 years is essentially 50% with approximately 12,000 deaths each year. The highest incidence is reported for African American men over the age of 45 years. The major risk factors include tobacco products, and alcohol.

Smokeless tobacco use has a significant effect on children by inducing oral premalignant and malignant mucosal lesions, and localized gingivitis. In 1992, 32% of high school students in the United States have tried smokeless tobacco; most of these males. In 1993, a national survey of boys 9-12 years of age indicated, for example, that 40% used smokeless tobacco in West Virginia, 39% in Kentucky, 33.8 % in Tennessee, 26.2% in Arkansas and 16.2% in Illinois. The available evidence suggests that there is a continued increase in the use of smokeless tobacco products by adolescent children in this country. Contact carcinogenesis is the most likely mechanism that results in this type of oral cancer lesion; the smokeless tobacco constituents condense on the oral mucosal and gingival surfaces in those specific topographical regions where the tobacco product(s) is placed.

Tobacco is also the number one risk factor for periodontal diseases (e.g. gingival bleeding, acute necrotizing ulcerative gingivitis, and periodontitis) which afflict more than 50% of the adult US population. Periodontal disease is the primary cause of tooth loss; approximately

10% or 17 million American adults are edentulous. The burden of tooth loss and edentulism is greater than \$10 billion each year.

A recent study by the California Birth Defects Monitoring Program (1996) reported that mothers who smoked 20 or more cigarettes per day during the month before conception through the first three months of pregnancy were more than twice (2.6 times) as likely to have infants with cleft lip and palate. Those mothers who smoked less were about 1.5 times as likely to have infants with oral clefts. Cleft lip and palate costs are estimated to be \$1 billion per year in the US.

Scientific inquiry continues to identify additional diseases and disorders where tobacco products alone or in combination with other risk factors are implicated in a number of other diseases and disorders such as low birth weight and premature births, osteoporosis, oral candidiasis, aphthous ulcers, altered taste and smell acuity, and impaired soft and hard tissue wound healing.

Finally, a sound basis has been established for involving the oral health professions in addressing tobacco control programs and in documenting the use of tobacco products. One example of this collaborative effort is the partnership between NIDR and NCI, CDC, Robert Wood Johnson Foundation, Oral Health America, Major League Baseball in addressing the problems associated with "split tobacco." These initial efforts indicate that there is a strong capacity to extend the educational programs required to realize public cessation of tobacco use in this country, especially among youth.

B. Tobacco-Related Research of NIDR

Current NIDR-sponsored research related to tobacco and tobacco-related diseases includes research on smokeless and smoking tobacco, nicotine and other ingredients or metabolites of cigarettes, and studies that collect information on tobacco use or smoking history for tabulation or analysis. Research on tobacco totaled about \$2.5M which was about equally divided between basic and clinical research.

1. NIDR-Sponsored Basic Research

NIDR-sponsored basic tobacco-related research includes molecular genetics and cell biology. Most of these projects address tobacco/smoking and oral cancers: mechanisms of tumorigenesis and cell injury, clonality studies, replication error and DNA repair mechanisms. Others examine the effects of nicotine/tobacco on inflammatory mediators and immune cell function in periodontitis. Two studies are molecular epidemiologic, and one study assesses the role of tobacco in *Candida albicans* drug resistance in AIDS patients.

NIDR-sponsored clinical tobacco-related research includes case-control and longitudinal studies in humans to ascertain risk factors (one of which is tobacco use/smoking history) for adverse medical outcomes. Outcomes (listed in frequency order) are: oral cancer, periodontitis, skeletal and alveolar bone loss, and candidiasis. One study examines immunoglobulin levels after smoking cessation in successful versus recidivistic patients.

2. NIDR-sponsored behavioral research

NIDR-sponsored behavioral tobacco-related research includes one study of validation of self-reporting methods (patient recall of tobacco use) for retrospective analysis of risk assessment. Behavioral research is defined to include studies that addressed issues of why people smoke and how can we get them to stop. The validity of reports/estimates of smoking history are also included in this category.

3. NIDR-sponsored epidemiology/surveillance research

NIDR-sponsored epidemiology/surveillance tobacco-related research includes Several studies. One assesses drug use (including tobacco) by dentists and dental students. The other is a descriptive epidemiology study of the oral health of a defined minority population in which tobacco use/smoking history is one factor tabulated. In addition, NIDR sponsors the oral health component of the National Health and Nutrition Examination Surveys that include assessment of tobacco use as well as assessment of tobacco-related health effects.

4. NIDR Activities in Prevention

An example of NIDR activity in prevention is our collaboration with NCI focusing on "spit tobacco" educational initiatives targeted at children, adolescents, and young adults. With the help of role models from Major League Baseball, the key educational messages are as follows: spit tobacco is not a safe form of tobacco, spit tobacco is addictive, and spit tobacco use can lead to cancer and other health problems. This collaboration has produced a variety of educational, informative and motivational materials as brochures, baseball player trading cards, posters, a video and a teacher's guide.

5. NIDR-Sponsored Research on Tobacco-Related Diseases

NIDR-sponsored research on diseases that are impacted by tobacco totaled about \$45M. Of this research, 82% was classified as basic research and 14% as clinical. The three primary program areas that comprise NIDR's tobacco-related disease research include oral, pharyngeal and nasopharyngeal cancer, periodontal diseases and craniofacial birth defects.

C. NIDR Plans for Expanded Tobacco-Related Research

There needs to be an extensive increase in basic, translational, patient-oriented and community-based research in each of the three major areas outlined above: oral cancer, periodontal diseases and craniofacial birth defects. The PHTF could enable this increase to occur. For example, the molecular mechanisms are not as yet known for how specific tobacco ingredients cause oral neoplastic lesions, effect opportunistic oral microbes associated with gingivitis and periodontal diseases, or produce cleft lip and/or palate during the first trimester of human pregnancy. Sensitive and specific diagnostics are not available to identify tobacco-induced premalignant oral, pharyngeal, nasopharyngeal or laryngeal lesions, or to identify individuals highly at risk for tobacco-induced destructive periodontal diseases or craniofacial birth defects.

A substantial expansion of the Centers of Oral Cancer (co-funded with NCI) as well as support for increased investigator-initiated research using the resources of the PHTF could significantly enhance scientific progress towards understanding the natural history, etiology, molecular pathogenesis, diagnostics, therapeutics and prevention of tobacco-induced oral and pharyngeal cancers. Preclinical and clinical research should be significantly expanded, along with a major expansion of human behavioral research targeted to children and adolescents.

Specific efforts to define how tobacco constituents influence opportunistic oral microbe (viral, bacterial and yeast) pathogenicity as well as the host immune response should be increased and could be with resources from the PHTF. In addition, the basic science studies of how tobacco constituents effect bone formation and bone resorption should be expanded since this knowledge base is essential for the development of diagnostics and therapeutics for tobacco-associated periodontal diseases.

Specific efforts are needed to define how specific tobacco products effect maternal physiology associated with premature and low birth weight babies as well as craniofacial birth defects. In addition, high risk individuals need to be identified to enhance counseling efforts to reduce the burden of tobacco-associated birth defects. These approaches will require large and well-defined populations along with cost effective instrumentation and related technology for genotyping. The magnitude of this project will require funds such as those that could be made available from the PHTF.

Since monitoring of tobacco use is predominantly captured by self-report, the development of low cost and rapid salivary diagnostic tests to verify or validate use are needed. In addition, further development of salivary and other orally-related diagnostic tests for viral and other cofactors of diseases related to tobacco would permit more specific risk assessment of individuals and populations.

Behavioral and educational research efforts focused upon unique contributions to be made by health professions in tobacco control could further current efforts directed towards children. For example, 75% of children ages 3-17 years visit a dental office each year. Outreach of this magnitude would involve development, testing, production, storage, distribution, and assessment of interventions and/or educational material. Resources from the PHTF could enable this type of effort.

VII. NATIONAL INSTITUTE ON DRUG ABUSE (NIDA)

The mission of NIDA is to lead the nation in bringing the power of science to bear on drug abuse and addiction, through support and conduct of research across a broad range of disciplines and by ensuring rapid and effective dissemination and use of research results to improve prevention, treatment, and policy. The use of tobacco products is by far the Nation's deadliest addiction. Research conducted by the NIH has contributed to the Nation's overall understanding of nicotine as an addictive drug. The NIDA has taken the lead in developing pharmacological and behavioral treatments for nicotine addiction. Nicotine addiction, like other drug addictions, is characterized by uncontrollable, compulsive drug seeking and use, even in the face of negative health consequences. A testimony to this is the fact that most smokers identify tobacco as harmful and express a desire to reduce or stop use, with nearly 20 million of them making a serious attempt to quit each year. Unfortunately, less than 7% of those attempting to quit achieve even one year of abstinence, with most relapsing within a few days of attempting to quit. This exemplifies the growing need to develop new and improved strategies and treatments for nicotine addicts that will not only contribute to improving the overall health of the nicotine addict, but lower the overall health cost of the Nation. Because of NIDA's understanding of addiction, it can play a pivotal role in preventing and treating nicotine addiction. Critical scientific opportunities for research are outlined below.

A. Basic Tobacco-Related Research of NIDA

Nicotine is the primary component in tobacco that acts on the brain. NIDA supports basic research on neurochemical and molecular approaches to nicotine addiction, nicotinic receptors in the brain and the pharmacologic basis of nicotine addiction. NIDA also supports projects examining genetic differences in nicotine sensitivity as well as behavioral genetic studies of smoking behavior. NIDA also supports research on the treatment of nicotine addiction by focusing on the development of nicotine and non-nicotine replacement medications in combination with behavioral strategies. NIDA also supports studies on craving and individual and gender differences in cigarette abstinence.

NIDA has an ongoing program of health services research looking at access to, effectiveness, and cost-effectiveness of drug abuse treatment services in improving the health and social functioning of persons addicted to illicit and licit drugs including tobacco. In addition, NIDA supports research to increase patient engagement in the treatment process that leads to improved retention rates and lower rates of relapse to drugs of abuse following treatment.

Cigarette smoking is a complex behavior. Recognizing that behavioral interventions are the cornerstone of nicotine addiction treatment, NIDA's behavioral research on nicotine and smoking focuses on an understanding of the antecedents of tobacco use, and changing behavior patterns.

One of NIDA's most important goals is to translate research findings, especially those about the actions of drugs on the brain, to help the public better understand the nature of addiction and the most effective strategies for its prevention and treatment. NIDA carries out a large variety of programs to ensure the rapid dissemination of research information and its implementation in policy and practice. It also develops and disseminates science-based prevention strategies to communities throughout the country.

Current NIDA-supported epidemiological studies monitor patterns of drug use including nicotine, such as The Monitoring the Future Study that the Nation relies on for examining current drug use and trends among our Nation's youth. These studies provide invaluable data to inform development of prevention and treatment strategies. NIDA also has a rich portfolio of research on risk and protective factors, as well as studies on the co-occurrence of nicotine with other drugs of abuse.

B. NIDA Plans for Expanded Nicotine-Related Research

1. Nicotine Addiction

With resources made available through the PHTF, NIDA intends to significantly expand its study of nicotine as an addictive drug. Emphasis will focus on a number of specific areas including

the brain regions that are involved in mediating the reward and reinforcing properties of nicotine. In addition, brain mechanisms of nicotine action will be explored with the goal of identifying specific brain receptor subtypes that mediate aspects of addiction and craving. It is clear that susceptibility to nicotine addiction is variable in the population. Although undoubtedly a complex phenomenon, it is likely the genetic differences play a role. The genetics of complex behaviors is beginning to be unraveled in a number of instances. It is the goal of NIDA to map and identify all of the genes contributing to vulnerability to nicotine addiction. While this is an ambitious goal, the PHTF could enable it to be realized.

2. Nicotine's Consequences

The interaction between nicotine and other drugs is also of interest to NIDA. With PHTF resources, NIDA will support research related to the "gateway hypothesis" that envisions the brain as being primed by one drug for other drugs. NIDA will support studies examining whether nicotine primes the brain for other drugs of abuse and the role that compounds such as caffeine play in priming individuals for nicotine addiction.

The developmental consequences of nicotine exposure are of profound importance given the significant degree of exposure that occurs in utero and during the critical developmental period following birth. Estimates are that greater than 40% of infants live with at least one smoker. The PHTF will enable large-scale studies needed to examine the peri- and prenatal effects of nicotine exposure, the long-term developmental consequences of nicotine on the brain, and vulnerability to subsequent nicotine addiction after exposure to nicotine in utero.

NIDA will also utilize PHTF resources to expand support for investigation of nicotine's effects on cognition and the effects of chronic nicotine exposure on brain function. The role that cognitive effects such as heightened alertness, sustained performance levels, and enhanced memory have in the development of dependence are complex and will require large-scale studies to unravel. Studies on observed changes in receptor function after chronic drug exposure are needed to understand the maintenance of smoking behavior.

C. NIDA Plans for Expanded Clinical and Treatment Research

NIDA currently supports research on the treatment of nicotine addiction by focusing on the development of nicotine and non-nicotine replacement medications in combination with behavioral strategies. Individual and gender differences in cigarette abstinence are being examined, but the PHTF could enable these efforts to be enhanced.

1. Medication Development

NIDA will employ PHTF resources to examine non-nicotine, non-addictive medications for nicotine addiction. Basic research is needed for the development of non-nicotine, non-addictive drugs that target molecular sites other than nicotine receptors (e.g., Wellbutrin®). NIDA will also expand research on nicotine replacement therapies focusing on novel nicotine-like compounds which act at nicotine cholinergic receptors and produce nicotine replacement as well as blockade.

Tobacco contains many chemicals in addition to nicotine. Recent neuroimaging studies have shown that smokers have significantly lower monamine oxygenase A and B (dopamine metabolic enzymes) levels than either ex-smokers or nonsmokers. It is critical to understand how components other than nicotine may contribute to the development of the addiction process, to sustained smoking behavior, and to develop treatments focusing on those components. The PHTF could enable a substantial enhancement of studies on the non-nicotine psychoactive components of tobacco.

2. Multicenter Clinical Treatment Trials

NIDA will utilize PHTF resources to enable multicenter clinical trials for the treatment of nicotine addiction. Interventions aimed at children and adolescents is crucial. An amazing 89% of all adult smokers began smoking before age 18. PHTF resources will enable research aimed at the development of efficacious treatments (both behavioral and pharmacological) specifically for children and adolescents early in the course of their nicotine use.

Expanded research on the most advantageous integration of pharmacological and behavioral treatments for all smokers is essential. It is likely that the optimal combination of pharmacological and behavioral interventions differs among different groups of smokers. NIDA will seek to explore these difference. In addition to children and adolescents, interventions for pregnant women and other special populations including specific ethnic/racial groups will be explored.

Another important issue that can only be addressed in large-scale clinical trials of the kind that could be enabled by the PHTF is that of comorbidity. NIDA desires to support the examination of the potential links between tobacco use and psychiatric disorders and to develop targeted treatments based on these trials.

D. NIDA Plans for Expanded Health Services Research

Health services research looking at access to, effectiveness, and cost-effectiveness of drug abuse treatment services in improving the health and social functioning of persons addicted to illicit and licit drugs including tobacco is extremely important. The best of interventions is worthless if it cannot be delivered to individuals addicted to nicotine. NIDA supports such research along with research aimed at increasing patient engagement in the treatment process. Such engagement is known to lead to improved retention rates and lower rates of

relapse to drugs of abuse following treatment.

NIDA will utilize PHTF resources to expand research that will increase the transportability of efficacious therapies to the community/private practitioners. Of particular interest is the use of new technologies to enhance access to interventions. Among the technologies that will be the subject of this research will be hand-held computers for delivery of smoking cessation interventions. NIDA will also support research aimed at the use of telephone interventions (e.g., hotlines) as well as Web-based interventions to advise those trying to quit on their own.

Additional research is needed to define the primary care needs of individuals with nicotine addiction. The PHTF will enable research on screening instruments that assess primary care needs among smokers aimed at matching patient needs with appropriate levels of care. It is also critical to recognize the barriers to treatment that exist within distinct population groups and to explore means for lowering these barriers. In the era of managed care, it is particularly necessary to identify the most cost-effective interventions in the context of a larger public health approach to nicotine addiction. To be cost-effective, treatments must be first and foremost be effective. Attempts simply to cut costs can result in inferior treatments if research is not conducted into the type of training and credentialing that is necessary in order to assure quality treatment. NIDA would conduct this type of research with resource from the PHTF.

E. NIDA Plans for Expanded Behavioral Research

Everyone agrees that cigarette smoking is a complex behavior and that behavioral research is a critical component of dealing with nicotine addiction. NIDA's behavioral research on nicotine and smoking will continue to focus on an understanding of the antecedents of tobacco use, and on means of changing behavior patterns. This research will explore the most effective images and communication modes for more strategic and effective antismoking media campaigns in children and adolescents.

While much research is dependent upon experimentation involving humans, NIDA will use PHTF resources to identify animal models that capture certain components of behavior related to tobacco use. These will include examinations of conditions under which stress causes nicotine tolerance and relapse to nicotine use.

Like all aspects of smoking, abstinence and withdrawal are complex. Because most smokers try to quit but fail, it is important to conduct research aimed at understanding the functional impairments such as psychomotor and cognitive functions that smokers experience during abstinence and withdrawal as primary factors in relapse. The PHTF could enable this critical research to be conducted quickly thereby increasing the success rate of smokers who are trying to deal with their addiction. Even among those who are not committed to quitting tobacco use, this research may influence levels of consumption. It will be important to assess craving levels in controlled and real life settings to develop better interventions.

F. NIDA Plans for Expanded Public Health and Community Research

One of NIDA's most important goals is to translate research findings, especially those about the actions of drugs on the brain, to help the public better understand the nature of

addiction and the most effective strategies for its prevention and treatment. This entails a large variety of programs to ensure the rapid dissemination of research information and its implementation in policy and practice.

In order to develop and disseminate high-quality, science-based prevention strategies to communities throughout the country, research is needed to guide the refocusing of current successful drug use prevention strategies on nicotine and to target interventions to particular populations including children and adolescents. The tobacco industry has spent billions of dollars on advertising to promote tobacco use, and these advertising campaigns were based on research. As the NIDA seeks to disseminate information regarding the kicking of the tobacco habit, it is no less important that these information campaigns be based on methodologies with demonstrated success. The PHTF would enable NIDA to pursue research that will aid in the development of materials that effectively focus on nicotine as an addictive substance and to develop effective media campaigns to foster the dissemination of information on the addictive nature of nicotine.

G. NIDA Plans for Expanded Surveillance/Epidemiology Research

NIDA-supported epidemiological studies monitor patterns of drug use including nicotine, such as The Monitoring the Future Study that the Nation relies upon for examining current drug use and trends among our Nation's youth. These and additional studies supported by the PHTF will provide invaluable data to inform development of prevention and treatment strategies. NIDA seeks to enhance its portfolio of research on risk and protective factors, as well as studies on the co-occurrence of nicotine with other drugs of abuse.

What are the risk factors that impact on tobacco use? The PHTF will enable research aimed at answering this complex question. Research will examine multiple levels of risk factors, including larger socio-environmental factors such as price, exposure to advertising, and promotional activities, ethnic influences, and affective states. Critical will be an expansion of surveillance systems to measure knowledge, attitudes, and behaviors regarding tobacco use among adolescents and adults. Large, population-based, longitudinal studies are needed to assess determinants of initiation and cessation of tobacco use. The PHTF could enable this research as well as provide the opportunity for epidemiological research on tobacco use as a comorbid disorder with mental disorders or as an antecedent to other drug use.

VIII. NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES (NIEHS)

The mission of the National Institute of Environmental Health Sciences (NIEHS) is to reduce the burden of human illness and dysfunction from environmental causes by understanding each of these elements and how they interrelate. The NIEHS achieves its mission through multidisciplinary biomedical research programs, prevention and intervention efforts, and communication strategies that encompass training, education, technology transfer, and community outreach.

A. Tobacco As An Environmental Hazard

Tobacco, particularly tobacco smoke, is a critical public and environmental health problem. Smoking is linked to cancers of the lung, esophagus, oral cavity, pancreas, kidney, and bladder, accounting for an estimated 30% of all cancer deaths. Smoking during pregnancy is linked to miscarriage and low birth weight in infants. Smoking contributes substantially to the risk of cardiovascular disease (coronary artery disease, stroke, and high blood pressure) and is the leading cause of chronic lung disease, responsible for 90% of deaths from chronic obstructive pulmonary disease (COPD). In addition, exposure to environmental tobacco smoke (second-hand smoke) is estimated to cause approximately 3,000 lung cancer deaths per year among nonsmokers and contribute to as many as 40,000 deaths related to cardiovascular disease.

This existing body of knowledge may be sufficient to drive a new wave of smoking cessation efforts, but there is still a great deal of research to be done which will ultimately shape our focus as public health practitioners, leading us to new prevention strategies, new target populations, and new interventions for tobacco-related morbidity and mortality. We need to understand better how tobacco and tobacco smoke exert their effects at the cellular and genomic level. We need to examine the effects of tobacco components on the endocrine and immune systems, with emphasis on developmental effects, effects of repeated exposures, and roles of inflammatory cells in generation of adverse health effects. We need a better understanding of susceptibility to tobacco smoke and its effects, including nicotine addiction. We need more research on the interactions of tobacco components and tobacco smoke with other environmental agents such as radon and air pollutants. Exposure to tobacco smoke in the home is already identified as a risk factor for development of asthma in children; continued study of tobacco smoke as an environmental factor in asthma and other multifactorial diseases may uncover additional, currently unsuspected health effects of tobacco that will drive our public health strategies in the future.

B. Tobacco-Related Basic Research of NIEHS

NIEHS has a long history of research on the numerous carcinogenic components of cigarette smoke such as benzo[a]pyrene and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone, their metabolism and distribution in the body, and their ability to interact with, and damage DNA, leading to cancers. Building on this early body of work, NIEHS scientists are increasingly defining how genetic differences in the ability to metabolize cigarette smoke carcinogens confers individual risks to cancer. For example, NIEHS scientists showed that differences in the gene coding for the carcinogen metabolism enzyme glutathione S-transferase M1 could increase the risk of bladder cancer by 70% in smokers. These types of correlations between genetic differences in metabolizing enzymes and cancer risk are being attempted on a host of cancers, including those of the lung, prostate, breast, colon, and anogenital tract.

Cigarette smoke carcinogens operate in a multi-step process that involves interacting with, and damaging, critical strands of DNA. NIEHS has supported a number of studies that investigate this process, including the mechanisms by which the human body corrects any errors arising from carcinogen-DNA adducts, and the consequences when DNA repair mechanisms are unable to detect or repair damage. Important work in this area includes a recent study that identified the actual areas on the tumor suppressor gene, *p53*, that were preferentially attacked by the cigarette carcinogen benzo[a]pyrene. These sites were the exact areas that are found damaged in lung cancer patients, thus providing an early mutational "fingerprint" of subsequent lung cancer risk. Work of this nature gives valuable insight into the molecular mechanisms by which chemicals found in cigarette smoke can exert biological damage.

One of the greatest tragedies of cigarette smoking is that it can have adverse effects on children exposed to second-hand smoke. Maternal smoking is suspected of negatively affecting formation of the placenta and of causing premature separation of the placenta, resulting in perinatal morbidity and neonatal mortality. Pregnant women who smoke are twice as likely to give birth to infants with a harelip birth defect and their children are at greater risk of being born with low birth weight. The developing lungs and nervous system of the young are also suspected of being unusually vulnerable to even low levels of environmental tobacco smoke. The NIEHS is funding studies to investigate the impact of maternal smoking during pregnancy on the infant and child. In one study, rats are being used to determine if passive maternal smoking affects the neurobehavioral development of the fetus and subsequent cognitive development of the young animal. Of particular interest in this study are any structural and functional disruptions of the hippocampus. Such detailed study may in future lead to strategies by which these adverse effects could be circumvented or reversed.

C. Tobacco-Related Epidemiology/Surveillance Research of NIEHS

NIEHS researchers have long been interested in how tobacco smoke can potentiate the action of other known environmental carcinogens. For example early work on the fatal pulmonary cancer, mesothelioma, showed that it was caused by the insulating material, asbestos. When workers were exposed to both asbestos and tobacco smoke, their risk of developing mesothelioma was greatly enhanced. NIEHS epidemiologists are investigating whether concurrent exposure to tobacco smoke increases cancer risks from household radon exposures and other environmental exposures.

D. NIEHS Plans for Expanded Tobacco-Related Basic Research

The proposed Environmental Genome Project would provide a unique mechanism to increase our knowledge of specific genes affected by components of tobacco smoke and of the variability within the human population in susceptibility to these chemicals. This project will be a multicenter effort to obtain information on DNA sequence diversity for the U.S. population on genes currently recognized to affect susceptibility to environmental disease. This is an extremely ambitious but very doable project. The rapidity of its completion would be greatly enhanced by resources of the PHTF.

The effects of involuntary exposures to tobacco smoke on the fetus, infant, and child remains an important research area. It is particularly important to understand the vulnerability of the

developing lung and nervous system to tobacco smoke and the long-term consequence of these early exposures. Other important non-cancer endpoints include immune suppression and bone development. The PHTF could enable this important research.

The mechanisms by which tobacco smoke increases a woman's risk of the crippling bone disorder, osteoporosis, need to be defined. NIEHS-supported research suggests that cadmium delivered in the smoke stream might be the component most responsible for this disease. More research is needed.

Other important biological mechanisms to be explored include the effect of tobacco smoke on oxidative stress, inflammatory responses, immunosuppression, and disruption of hormonal homeostasis. Work also needs to be continued at the genomic level to identify mutational "hot spots" that are particularly vulnerable to attack by components of tobacco smoke. Study on the mechanistic components of tobacco exposure will provide insight into new health effects from tobacco smoke, into how tobacco smoke interacts with other environmental agents to potentiate adverse health effects, and into promising strategies for preventing, circumventing, or reversing these adverse effects. The PHTF could enable this research.

The PHTF could also support the identification of additional biomarkers of tobacco-related exposures and effects. These biomarkers could be used as "early warning systems" to alert individuals about impending disease development if they continue smoking. This might prove one of the most useful tools for encouraging smoking cessation since it would identify the actual risk that an individual has, rather than extrapolating from aggregated population studies.

E. NIEHS Plans for Expanded Tobacco-Related Epidemiology/Surveillance Research

With PHTF support, epidemiology studies could be expanded to investigate other disease endpoints for which concurrent exposure of tobacco smoke and environmental exposures confer greatly increased risk over single exposures. Additionally promising biomarkers of exposure and of genetic susceptibility could be incorporated into epidemiology studies to give a level of refinement and precision not previously possible in identifying health risks associated with tobacco smoke. The utility and precision of epidemiology studies on tobacco smoke could also be greatly enhanced by including markers of genetic susceptibility.

IX. SUMMATION OF THE PERSPECTIVE OF THE NIH ON THE PHTF

It should be abundantly clear from this document that there exists no shortage of worthy research projects aimed at reducing tobacco use and reducing the burden of tobacco-related diseases. Many of these research projects are of such a magnitude as to make them difficult to envision apart from additional resources. The Public Health Trust Fund could enable these projects to move from dreams to reality.

The millions of lives already lost to tobacco ought not to be followed by millions more. These deaths are largely preventable. The negative economic impact of tobacco that accompanies its wave of death and disability is also avoidable. There are things that can be done. Only some have been described in this document. The National Institutes of Health has been the leader in tobacco-relevant research and is positioned to continue to lead in the years ahead.

If the resources of the Public Health Trust Fund are large enough, if these resources are sustained, and if proper stewardship is exercised, its establishment may one day be viewed as among the most significant events in the history of public health.

DRAFT (July 9, 1997)

SMOKING CESSATION & EDUCATION
Workgroup Consensus: Highlights

Scope of the Problem:

- ▶ There are approximately 50 million smokers, and about 20 million would like to quit. The settlement provides substantial funds to help them do so.
- ▶ There is a direct relationship between cessation of tobacco use and public education, therefore, public education will be treated as an integral component of any approaches designed to reduce the use of tobacco products.
- ▶ Cessation and education strategies must take into account that smoking is an addiction, therefore, it should not be anticipated that success rates for cessation treatments will be comparable to those for more acute processes such as antibiotics for infections. Instead, cessation programs should be regarded in the same light as other chronic conditions such as diabetes, and their success should be held to similar standards.

Settlement Funds Available: In addition to funds specified for cessation and education activities, we should consider crossover with other funding streams, i.e., "Teams' Fund" (\$1.8 billion), and Public Health Trust Fund (\$25 billion):

Funding Mechanisms/Decisionmaking:

- ▶ Mechanisms of administration of settlement funds (e.g., government versus nonprofit entity versus combination of different mechanisms separating control to different pots of money as an accountability feature).
- ▶ Need for investment, decisionmaking and priority-setting mechanisms.
- ▶ Federal programs (NIH ASSIST, CDC IMPACT, ungirded by the funded state and local programs (including school-based programs) can provide infrastructure for new activities--broader program implementation, permitting local control and input, tailored to local needs. Need to look at states that spend more per capita and have more effective programs (e.g., California and Massachusetts).
- ▶ Tribes - the settlement treats tribes like states, but the formula is based on tribal population as a percentage of state population, thus not providing adequate funds for successful program implementation.

Spending Priorities:

- ▶ A lot is known about education and cessation program effectiveness (see attachments). There is an issue about whether to use funds to invest in areas (education and assistance) that create demand for cessation services/products or on service delivery or programs that are or could/should be provided by others (particularly the private sector). In areas where we do fund services, those services should be targeted on certain subpopulations.
- ▶ Need to develop effective cessation programs for youth (controversial, e.g., use of nicotine replacement products).

- ▶ Some portion of cessation and education money needs to go to teach clinicians (nurses and doctors) and managed care plans as to how to encourage smoking cessation.
- ▶ There is some evidence that although it costs more to provide cessation services to more individuals, after a certain point there is an economy of scale, and costs per individual begin to decrease so that the overall program is more cost-effective (i.e., the higher the investment, the more return you probably will see per dollar invested).

Research Needs: Necessary crossover with Settlement's research funding.

- ▶ Need for market analysis for private sector delivery of cessation programs/products--government does not necessarily need to supplant current market demand. In addition, need analysis of insurance plan cessation programs, reimbursement, incentives. Currently, all insurance companies have some sort of limit on cessation programs (e.g., in the form of co-pays and/or limits on the number of visits).
- ▶ Need to characterize why it is so hard to get people into intensive treatment (lack of access when they are ready? too complicated to enter the system?).
- ▶ Need market research on nicotine replacement market (one company spends \$120 M on PR alone for product, profits must be much higher). Specific concern that minorities and lower-income people cannot afford these techniques.

MAKING THE CASE FOR SMOKING CESSATION

Evidence from the AHCPR Smoking Cessation guideline suggests that tobacco use presents a rare confluence of circumstances:

- 1) a highly significant health threat
 - 2) a disinclination among clinicians to intervene consistently
 - 3) the presence of effective, preventive interventions
- 50 million Americans smoke - 20 million of those want to quit each year
 - Direct health costs of smoking are \$50 billion annually - - every 1 million smokers who quit represents \$1 billion less spending on direct health costs and about the same savings in indirect costs.
 - Currently 1.3 million smokers quit on their own each year - AHCPR Smoking Cessation guideline will, conservatively, double the quit rate annually.
 - This translates into an additional savings in the health care sector of \$1.3 billion annually
 - Approximately 1 million young people start smoking each year. Best case scenario - prevention campaign would reduce that number by 50%
 - Widespread implementation of the AHCPR Smoking Cessation guideline will more than double the return on our investment

NATIONAL CESSATION CAMPAIGN

- While we need to target both smokers and clinicians using an integrated, comprehensive approach - a 5 year national campaign focusing on cessation, the AHCPR initiative focuses on the clinician and his/her contact with smokers..
- At the clinical level, with the objective of changing attitudes and practice to recognize and treat smoking as a *chronic* disease, similar to diabetes and hypertension.
- At the consumer level to educate and empower patients to better understand their disease and how to overcome their addiction.
- Clinicians are in the most influential position to help patients and have direct access to the smoking population. They have a window of opportunity to identify and treat patients who smoke. Seven out of ten smokers see their physician annually.
- There are myths and misperceptions that keep clinicians from intervening and treating nicotine addiction in their patients - from pessimism about a smoker's ability to change his/her lifestyle, to not knowing what does and doesn't work to help people quit.
- There are 3.8 million health care providers in the nation.
- The National Cancer Institute projects that if 100,000 physicians were to help 10% of their patients quit each year, the number of smokers in the U.S. would drop by an additional 2 million. Even greater cessation would occur if other types of health care clinicians would also intervene with their patients who smoke.

CESSATION IS A GOOD INVESTMENT

- AHCPR guideline is the only guideline that provides evidence-based recommendations on what works and doesn't work for smoking cessation treatment.
- Compared to other preventive interventions, smoking cessation is extremely cost effective.

SEE TABLE 8

- The more intensive the intervention, the lower the cost per quality of adjusted life years (QALY) saved - suggesting that greater spending on interventions yields more net benefits (Fiore, et al).
- Cost to implement the AHCPR Smoking Cessation Guideline is \$8.1 billion in the first year - with a savings of \$2.6 billion in the first year. *→ all smokers*
- *→ \$2.5 - 1/3 try to quit each year.*
- Therefore, the funds that are tentatively set aside for the Public Health Trust Fund are inadequate - they provide only about one-tenth to one-fifth of an approximately applied cost of reimbursement.
- If 20 million smokers try to quit each year - providing \$500 each would cost \$10 billion - considerably more than the \$1.5 billion in the public health trust fund.

IMPLEMENTATION OF SMOKING CESSATION INITIATIVES

- In a recent survey, only 17% of managed care plans knew what percentage of their members smoke; only 15% could identify those members and only 18% have analyzed the financial impact of smoking to their organizations. (Pinney & Associates)

TABLE 8

COMPARISON OF SMOKING CESSATION COST-EFFECTIVENESS RATIOS WITH OTHER MEDICAL INTERVENTIONS

SELECTED INTERVENTIONS		
Intervention	Source	Cost-Effectiveness Ratio
Cholestyramine/low cholesterol diet (versus diet) for men aged 35-39 & 290/dL	Oster, <i>et al.</i> (1987)	102,033
Annual mammography & breast exam for women 40-49	Eddy, <i>et al.</i> (1988)	61,744
Hypertension screening for asymptomatic men age 40	Littenberg, <i>et al.</i> (1990)	23,335
Beta-blockers for low-risk myocardial infarction survivors	Goldman, <i>et al.</i> (1988)	16,897
3-vessel coronary artery bypass graft surgery (versus medical management)	Weinstein, <i>et al.</i> (1980)	12,350
PTCA (versus medical management) for men age 55 with severe angina	Wong, <i>et al.</i> (1990)	7,395
AHCPR Guideline, Combined Smoking Cessation Interventions	Cromwell, <i>et al.</i> (1996)	2,875
One time cervical cancer screening for women age 65+	Fahs, <i>et al.</i> (1992)	2,053
Pneumonia vaccination for people age 65+	Sisk, <i>et al.</i> (1983)	1,769
Polio immunization for children age 0-4	Sisk, <i>et al.</i> (1983)	<0

- Providing technical assistance for managed care organizations that serve populations with high incidence of smoking or who have made smoking cessation a priority.

Phase IV: Evaluation

- Evaluate efficacy of smoking cessation interventions
- Conduct needs assessment for clinics treating underserved populations and consider supplemental funding
- Managed care utilization survey (similar to Pinney's)
- Provide results to physicians so they can see immediate impact
- Direct-to-consumer survey on perceptions of smoking, cessation, etc.
- Provider survey (attitudes and assessment)
- Evaluate emerging populations of smokers (college students, etc.) to assess smoking cessation needs

Cost:

- Option 1 \$100 million over 5 years (\$20 million per year) -- drawing \$50 million from the public education campaign (item C) and another \$50 million from item #4
- Option 2 \$50 million over 5 years (\$10 million per year) -- splitting item #4 with prevention (100 million total budget)

- Educate the medical community about the guideline, its specific recommendations and provide tools that can help them with effective smoking cessation strategies for their patients.
- Educate medical and health schools to look at smoking status as a **vital sign**, teach proper counseling skills, referring, etc.
- Launch campaign (AHCPR's Two-Three Campaign) to target clinicians with smoking cessation prompts and interventions for patients, follow-up and referral strategies, etc.
- Develop or fund one-stop-shopping community clinics that specialize in smoking cessation and provide diagnosis, treatment, support and follow-up for at risk populations
- Internet web site, chat rooms to ask the doctor, etc.
- Exhibits

Phase III: Implementation

- Develop and disseminate tools that can be used in the clinical setting:
 - Software programs
 - Physician education kits
 - Patient education kits, including special populations
 - Patient incentives/giveaways as motivators
 - Audio/visual aids
- Train-the-trainer programs
- CE/CME seminars
- Offer matching federal grants as incentive to managed care to implement AHCPR-sponsored Smoking Cessation guideline

SMOKING CESSATION CAMPAIGN FUNDING STRATEGIES

Phase I: Federal Funding for Smoking Cessation

- Matching grants to managed care plans, physician groups, and other providers and plans to implement and/or evaluate the efficacy of smoking cessation interventions.
- Provide direct funding to Community Health Centers and other direct providers of care to populations served by HHS.
- Provide matching grants to states to implement and/or evaluate smoking cessation interventions in the Medicaid population.

Phase II: Education and Training

- Continuous updating of the AHCPR guideline as new treatments are proven effective
- Research and evaluate the efficacy of new treatments
- Educate managed care organizations about the benefits of cessation to begin to implement the guideline into their programs
- Educate the medical community about the guideline, its specific recommendations and provide tools that can help them with effective smoking cessation strategies for their patients.

CAMPAIGN FUNDING

Phase II: Education and Training

- Continual updating of the guideline as new treatments are proven
- Research and evaluate new treatments that work (spray, antidepressants, etc.)
- Educate managed care organizations about the benefits of cessation to begin implementing the guideline into their programs.

Guiding Principles for Public Education in Tobacco Control

Public education efforts, including mass media campaigns, grassroots promotions, and other community tie-ins, are needed to denormalize and deglamorize tobacco use among young people, as well as to provide smoking cessation motivation and assistance to adults and to foster public support for smoke-free environments. Whereas a youth-only strategy may inadvertently position tobacco use as a "forbidden fruit," a strategy that includes counter-tobacco messages for all ages and populations can have a powerful impact on reducing the demand for tobacco products in society at large.

Evidence of Efficacy

- Analysis of multi-faceted youth tobacco use prevention programs shows that comprehensive education efforts, combining media, school-based, and community-based activities, can postpone or prevent smoking onset in 20 to 40 percent of adolescents.
- The Fairness Doctrine campaign of 1967-1970, the only sustained nationwide education effort to date, documented that an intensive mass media campaign can produce significant declines in youth and adult smoking.

Successful Campaign Characteristics

- To be effective over the long run, a national education campaign must be comprehensive, intensive, and sustained. (Note: "Campaign" is used here in its broadest sense as a counter-marketing effort that includes media-based and non-media-based approaches.)
- It must mimic national marketing campaigns, including those of the cigarette companies themselves: continued message variation, pulsed media placement patterns (based on seasonality and audience media habits), promotional tie-ins, and ongoing communications measurement and tracking.
- The campaign should be theory-based, drawing on the extensive literature on psychosocial risk factors for initiating, continuing, and stopping tobacco use.
- The campaign should maximize use of existing high-quality media materials produced by the government, voluntary agencies, and a number of individual states. A large collection is currently available through CDC's Media Campaign Resource Center for Tobacco Control.

Message Content and Appeals

- There is no single "best" motivator for preventing or reducing tobacco use. Campaign messages for both youth and adults should feature a variety of appeals (fear, humor, satire, testimonials, etc.) and executional styles.
- Messages should address tobacco control as both an individual behavior change issue and an environmental/public policy issue.
- Especially for the youth audience, the campaign should use nonauthoritarian appeals that avoid direct exhortations not to smoke.
- Smoking cessation messages for adults should increase motivation to quit and offer tips and referral information.
- Clean indoor air messages should focus on the health hazards of ETS exposure, particularly on infants and children, steps that individuals can take to reduce exposure, and actions that communities can take to enforce existing laws and regulations.

Exposure Levels

- On a per-capita basis, the Massachusetts media program would cost over \$600 million nationally but still fail to adequately target the ethnic diversity of the U.S.
- It is estimated that an annual budget of about \$150 million is needed for a year-round broadcast campaign to

achieve necessary message reach and frequency against a general teen (ages 12-17) audience -- to expose about 75% of U.S. adolescents to each campaign message 6 or more times. This amount is for national broadcast media buys only and does not include costs for production, other media placements, or state and community programs and the infrastructure to deliver them.

- Substantial additional resources -- even beyond \$500 million annually -- are needed to reach different demographic and developmental segments of youth, to reach adults with cessation and ETS messages, to communicate messages through non-broadcast media-based channels, and to conduct a variety of non-media-based education efforts.

Message Formats

- The mass media component of the campaign should feature a mix of TV, radio, print, and outdoor advertising that complement and reinforce each other.
- The campaign should also explore the various alternative media options available (e.g., movie trailers, Internet, other computer resources, video games, materials for schools and community groups). This consideration is especially important in view of today's increasingly fragmented media market.
- Campaign planners should explore the need for new and/or tailored materials for at-risk populations (e.g., ethnic groups, people with diabetes, etc.).

Source Identification of Messages

- Planning and implementation of the multi-media campaign should be tightly coordinated; however, messages should appear to be coming not from one monopolistic source, but rather from a variety of sources.
- Highlighting a single theme, tagline, identifier, or sponsor for the campaign may increase the likelihood that young people, in particular, will discount or discredit the messages.

Media and Non-Media Strategies

- Just as tobacco marketing increasingly has moved away from traditional mass media advertising toward targeted promotional activities, tobacco counter-marketing campaigns should consider a combination of media advertising and grassroots promotional approaches.
- The current Secretarial Initiative to Reduce Tobacco Use Among Teens and Preteens contains four strategies in addition to a paid counter-advertising campaign:
 1. Promoting positive alternatives to tobacco use through sports and other youth-centered activities -- including establishing a national "branding" campaign for a tobacco-free lifestyle.
 2. Empowering young people to address tobacco use among their peers.
 3. Deglamorizing tobacco use through a coordinated entertainment industry strategy.
 4. Involving parents and families in addressing tobacco use among young people.

National vs. State Campaigns

- A national media campaign can deliver message reach and frequency at greatest cost efficiencies. Nationally originated messages can have a powerful influence on the public's perceived tobacco control "agenda" and set an overall supportive climate for state and local tobacco control efforts.
- State and local campaigns are necessary for optimizing the behavior and policy change objectives of the national campaign. They should focus not on developing new creative materials, but on local media selection to reach at-risk populations (e.g., ethnic newspapers), for local tagging of messages, where appropriate (e.g., providing statewide toll-free telephone numbers), and for community education tie-ins to the national campaign (e.g., local radio promotions, local TV and radio talk shows, community T-shirt exchanges, referrals to local cessation services).
- Costs for state and local counter-marketing activities are considerable, perhaps equivalent to the costs for a year-round national media campaign.

Tobacco Use Prevention and Control Intervention Importance of State-wide Programs

Need for State-wide Programs

Effective implementation of tobacco use prevention and control requires a concerted, coordinated, and synergistic effort at the national, state, and community levels. The foundation for a nationwide infrastructure has been developed through the ASSIST and IMPACT programs. These programs serve as "delivery systems" to link individual states and local communities across the nation with federal agencies (CDC, NCI, FDA, SAMHSA), national media campaigns, and research institutions. This nationwide infrastructure also should extend to include partnerships with state departments of education, national organizations, private industry and others. The resources proposed in the settlement agreement will expand and sustain long-term funding of such state-based tobacco control efforts.

Evidence of Efficacy

Efforts to reduce tobacco use in the United States have shifted from primarily focusing on smoking cessation for individuals to populations-based interventions that emphasize primary prevention and reducing the health risks of exposure to environmental tobacco smoke. Interventions are targeted to both youth and adult tobacco users; youth and adult non-users; and the social and environmental factors that encourage and support the use of tobacco. Programs based upon these principles have been demonstrated to reduce per-capita consumption in Massachusetts, California, and the ASSIST states.

Key Program Components

The majority of tobacco control interventions focus on six key components:

- Prevention, including the restriction of minors' access to tobacco products;
- Treatment of nicotine addiction;
- Reduction of exposure to environmental tobacco smoke;
- Counter-advertising and promotion;
- Economic incentives; and
- Product regulation

Funding to state programs will sustain and expand support for the following activities:

- Developing state tobacco prevention and control plans;
- Building and strengthening coalitions to ensure community participation in the development of tobacco prevention and control programs;
- Establishing state health department infrastructure to include staffing, data collection and analysis, resource development, training, technical assistance, media campaigns, educational programs, cessation programs, enforcement, promotion and implementation of public health policies, fostering leadership and coordination, and applied research;
- Conducting surveillance and evaluation activities; and
- Funding local programs, including county governments, community organizations and schools.

Current ASSIST and IMPACT awards provide minimal funding for school-based prevention efforts. Schools are key partners, and should adopt curricula that have demonstrated effectiveness in reducing tobacco use behaviors. School-based tobacco use programs also should be integrated into comprehensive school health education programs. Finally, any school-based program must be an integral part of community-wide strategies, and likewise, any community-based efforts in tobacco use prevention and control should incorporate school initiatives into overall strategies.

The Secretary's Initiative to Reduce Tobacco Use Among Teens and Pre-Teens

Reducing teen tobacco use has been identified as a Secretarial priority for interagency action. The primary aim of this Initiative is to contribute to the achievement of the President's goal of reducing tobacco use among young people by 50% in seven years. The Initiative focuses on strategies to reduce the demand for tobacco products among young people. A nationwide infrastructure of state and community-based programs is essential to effective implementation of the Initiative.

The Secretary's Initiative represents an interagency effort involving ACF, FDA, HRSA, IHS, NIH, and SAMHSA, with CDC serving as the lead. It builds on the strengths and organizational missions of the collaborating agencies and will utilize the delivery systems and community-based mechanisms already in place through these agencies to deliver tobacco demand reduction programs. Key action areas addressed in the Secretary's Initiative are:

- Promoting positive alternatives to tobacco use through sports and other youth-centered activities;
- Empowering young people to address tobacco use among their peers;
- Deglamorizing tobacco use through a coordinated Entertainment Industry strategy;
- Implementing a paid counter-advertising campaign to change social norms about tobacco use; and
- Involving parents and families in addressing tobacco use among young people.

Challenges of Tobacco Control in a Post Settlement Environment

While the proposed settlement can produce important and sweeping changes in the national environment related to tobacco, much will still remain to be done at the state and local level. There would also be a need for enforcement of federal legislative mandates, or effort to pursue actions beyond these mandates that more specifically address local needs. Ultimately, tobacco prevention and control is and will remain a local issue, requiring local control and refinement. The proposed state tobacco prevention and control infrastructure will be the critical component enabling this type of local response and control.

Smoking Cessation: Summary
Office on Smoking and Health, CDC; July 7, 1997

- Smoking cessation is a critical component of comprehensive efforts to reduce tobacco use. Smoking cessation has major and immediate health benefits for people of all ages.
- 70% of all smokers want to stop smoking completely. Effective smoking cessation strategies have been identified, but expanded diffusion of these strategies is needed.
- The 1996 Agency for Health Care Policy and Research (AHCPR) guidelines review evidence on smoking cessation interventions. The results clearly showed that a variety of smoking cessation interventions are effective:
 - Simple advice to quit by a clinician (30% increase in cessation)
 - Individual and group counseling (doubles cessation rates)
 - Telephone hotlines/helplines (40% increase in cessation)
 - Nicotine replacement therapy (NRT) (up to double the cessation rates)
- Studies have shown that providing brief advice to quit smoking during routine office visits, follow-up visits about smoking, and prescribing NRT are more cost effective than commonly utilized screening tests and treatment of risk factors such as hypertension or hypercholesterolemia.
- In a 1995 survey of 105 larger HMOs, two-thirds reported offering some level of smoking cessation program or product as a covered member service; however, there were often restrictions on the use of the benefit. Indemnity plans and corporations who self-insure their health insurance benefits generally do not cover smoking cessation services.
- Currently, only six states' Medicaid programs cover the cost of over-the-counter NRT. Medicare does not pay for smoking cessation interventions or NRT.
- A cost analysis of the AHCPR guidelines estimated that cost per smoker would range from \$34.04 for simple advice to quit to \$271.81 for individual intensive counseling plus nicotine gum.
- Paying for smoking cessation behavioral intervention and NRT increases use of these services. One study found that the increased costs of full coverage were commensurate with increases in cessation (e.g., 50% increase in cost = 50% increase in cessation).
- Longitudinal follow-up of adult smokers have shown that making more than one quit attempt approximately doubles the rates of successful quitting. Successful ex-smokers typically have attempted to quit but relapsed several times prior to quitting permanently. Therefore, restrictions on coverage of services needs to be carefully considered.
- Cessation services can be institutionalized through dissemination of the AHCPR guidelines, development of office systems to assess tobacco use as a vital sign with appropriate follow up, reimbursement for treatment, accountability for and measurement of cessation efforts.
- Current research indicates that adolescent smokers frequently try to quit but are usually unsuccessful, have withdrawal symptoms similar to adults, are hard to recruit and retain in formal cessation programs, and are not responsive to programs developed to date.

Smoking Cessation: Background Information

Office on Smoking and Health, CDC; July 7, 1997

Introduction

Smoking cessation is a critical component of comprehensive efforts to reduce tobacco use. Smoking cessation has major and immediate health benefits for men and women of all ages. For example, persons who quit smoking before age 50 have 1/2 the risk of dying in the next 15 years compared with continuing smokers (1990 SGR). 70% of all smokers want to stop smoking completely (MMWR 1996); however, nicotine is an addictive substance (1988 SGR), and only 2.5% of smokers stop smoking permanently each year (MMWR 1993). Effective smoking cessation strategies have been identified, but expanded diffusion of these strategies is needed.

What works for smoking cessation?

In 1996, the Agency for Health Care Policy and Research (AHCPR 1996) produced an evidence-based guideline that evaluated smoking cessation interventions available at the time. The results clearly showed that a variety of smoking cessation interventions are effective:

- Simple advice to quit by a clinician (30% increase in cessation)
- Individual and group counseling (doubles cessation rates)
- Telephone hotlines/helplines (40% increase in cessation)
- Nicotine replacement therapy (NRT) (up to double the cessation rates)

The guidelines also noted the following:

- The efficacy of intervention increases with intensity of intervention.
- Cessation treatments (both pharmacotherapy and counseling) should be provided as paid services; providers should be reimbursed for delivering smoking cessation interventions.

Intensive services (e.g., NRT plus behavioral counseling) have been proven to be effective with more heavily addicted smokers (Silagy 1994, Tang 1994)

What is the cost of providing smoking cessation interventions?

- Group Health Cooperative has implemented a behavior modification support program provided either through a series of brief proactive phone calls or via group meetings. This intervention may include a recommendation for NRT use (about 60% of participants used NRT).
- The total cost of the program was \$150 for the behavior change intervention and \$67 for the NRT; since not everyone used NRT, the average cost of delivery of the more intensive intervention was \$192.

- Some plans reimburse for services that are provided in the community (as opposed to services provided through the plan). For example, one plan reimbursed on average \$165-185 for cessation services provided through community channels. A cost analysis of the AHCPR guidelines estimated that cost per smoker would range from \$34.04 for simple advice to quit to \$271.81 for individual intensive counseling plus nicotine gum (AHCPR, unpublished and confidential data).

What is the cost-effectiveness of smoking cessation interventions?

- Studies have shown that providing brief advice to quit smoking during routine office visits, follow-up visits about smoking, and NRT were more cost effective than treating mild or moderate hypertension, drug therapy for hypercholesterolemia, PAP tests, zidovudine therapy for asymptomatic HIV infection, and breast and colon cancer screening (Cummings 1989, Oster 1986, Tsevat 1992, Sofian 1995).
- The AHCPR-commissioned study on the cost effectiveness of implementing the AHCPR smoking cessation guidelines also showed that more intensive interventions are more cost-effective than briefer interventions. The cost per year of life saved (at 5% discount) ranged from \$1582.19 for intensive group counseling without NRT to \$6830.84 for minimal counseling (<3 minutes) and nicotine gum (AHCPR, unpublished and confidential data).

What works regarding smoking cessation in children and adolescents?

Three out of four teens who smoke have made at least one serious, yet unsuccessful, effort to quit (NCHS, 1992). Current research indicates that adolescent smokers frequently try to quit but are usually unsuccessful, have withdrawal symptoms similar to adults, are hard to recruit and retain in formal cessation programs, and are not responsive to programs developed to date. Few adolescent cessation programs have been developed, and even fewer have been studied and evaluated (SGR 94, IOM 94). Nicotine replacement therapy may have a role in helping adolescents quit tobacco use. FDA has not approved it for use in those persons under age 18; however, there are isolated programs throughout the country that are either prescribing or distributing the nicotine "patch" and reporting high success rates in adolescents (Florida, State Dept of Health; Stotts C, unpublished and confidential data).

What is the current status regarding provision of smoking cessation interventions?

- Managed care plans and insurers tend to restrict access to cessation services, suggesting that their primary concern is about controlling drug and program utilization and cost, rather than getting smokers to quit.

- In a 1995 survey of 105 larger HMOs, two-thirds reported offering some level of smoking cessation program or product as a covered member service (Corporate Health Policies Group 1995). However, indemnity plans are least likely to cover preventive services (Schlauffler 1993). In addition, over half of corporations self-insure for their employees' health insurance benefits; few corporations include coverage for smoking cessation services in their health insurance benefit designs (Schlauffler 1993).
- Only 17% of the HMOs know what percentage of their members smoke, only 15% can identify those members who smoke, and only 18% have analyzed the financial impact of smoking to their organization.
- In 1995, over half (64%) of plans provided some coverage for the nicotine patch, but only about half covered it for all of their members. Also, the patch was covered as a standard drug benefit (treated like any prescription drug) by only 36% of plans that covered it. Since NRT has gone over-the-counter, it appears that fewer plans cover the patch, although a formal survey has not been done.
- In many cases, procedures were burdensome to receive coverage (e.g., completion of a smoking cessation program in order to be reimbursed or restrictions on the number of times the benefit could be used). In some cases, reimbursement was only provided if the individual stayed quit for a certain amount of time (e.g., six months).
- Nicotine gum was covered by fewer plans but fewer restrictions were placed on its use.
- In 1995, only about half of the plans offered a behavioral smoking cessation program in house; staff and group model plans were much more likely to provide these than network or IPA model plans (yet network and IPA models predominate the managed care market). While most plans do refer members to outside programs, only 32% of those who refer cover any portion of the cost of those programs.
- Currently, only six states' Medicaid programs cover the cost of over-the-counter NRT.
- Medicare does not pay for smoking cessation interventions or NRT.

Does paying for smoking cessation interventions improve cessation rates?

- Paying for smoking cessation behavioral intervention and NRT increases use of these services.

- One study found that quit rates were somewhat lower among persons who received full coverage for the services compared with those who had only partial coverage. However, because more individuals used the services when they were fully covered, full coverage had a higher overall impact on the population of smokers: a 50% increase in number of persons who quit. Full payment for the intervention and NRT also increased the cost by 50%; therefore, any increase in cost appears to be offset by a comparable increase in overall impact (Curry, unpublished and confidential data)
- Some plans only reimburse for cessation services if an individual stays quit for a certain amount of time (e.g., six months).

Is there a point of diminishing returns in providing smoking cessation services (e.g. should benefits only be allowed for a finite number of quit attempts)?

- Nicotine addiction should be viewed as a chronic disease. As with other chronic diseases, there may not be full patient compliance, and there may be remissions and relapses. However, for other chronic diseases, coverage is not restricted only to those who are fully compliant with treatment or to those put into permanent remission by the first course of treatment.
- Establishing a cut point for providing services does not make sense. Longitudinal studies have shown that the number of previous unsuccessful quit attempts was unrelated to success in quitting (Cohen 1989). One study suggests, in fact, that previous quit attempts may increase success rates (Hymowitz, unpublished and confidential data). Successful ex-smokers typically have attempted to quit but relapsed several times prior to quitting permanently (Cohen 1989, Fiore 1995).
- We do not know very much about how soon after an unsuccessful quit attempt a smoker will make another attempt. When smokers are asked when their last quit attempt was, the mean is about 3 years earlier (Gallup 1993). However, smokers often do not remember quit attempts that were of short duration that occurred more than few months previously (Pierce, 1994).
- We also do not know what effect the offer of more widely available treatment will have on quit attempts, particularly among highly dependent smokers. Clearly, greater access to NRT has resulted in greater utilization.

What is the data on the OTC patch use and use of adjunctive cessation assistance?

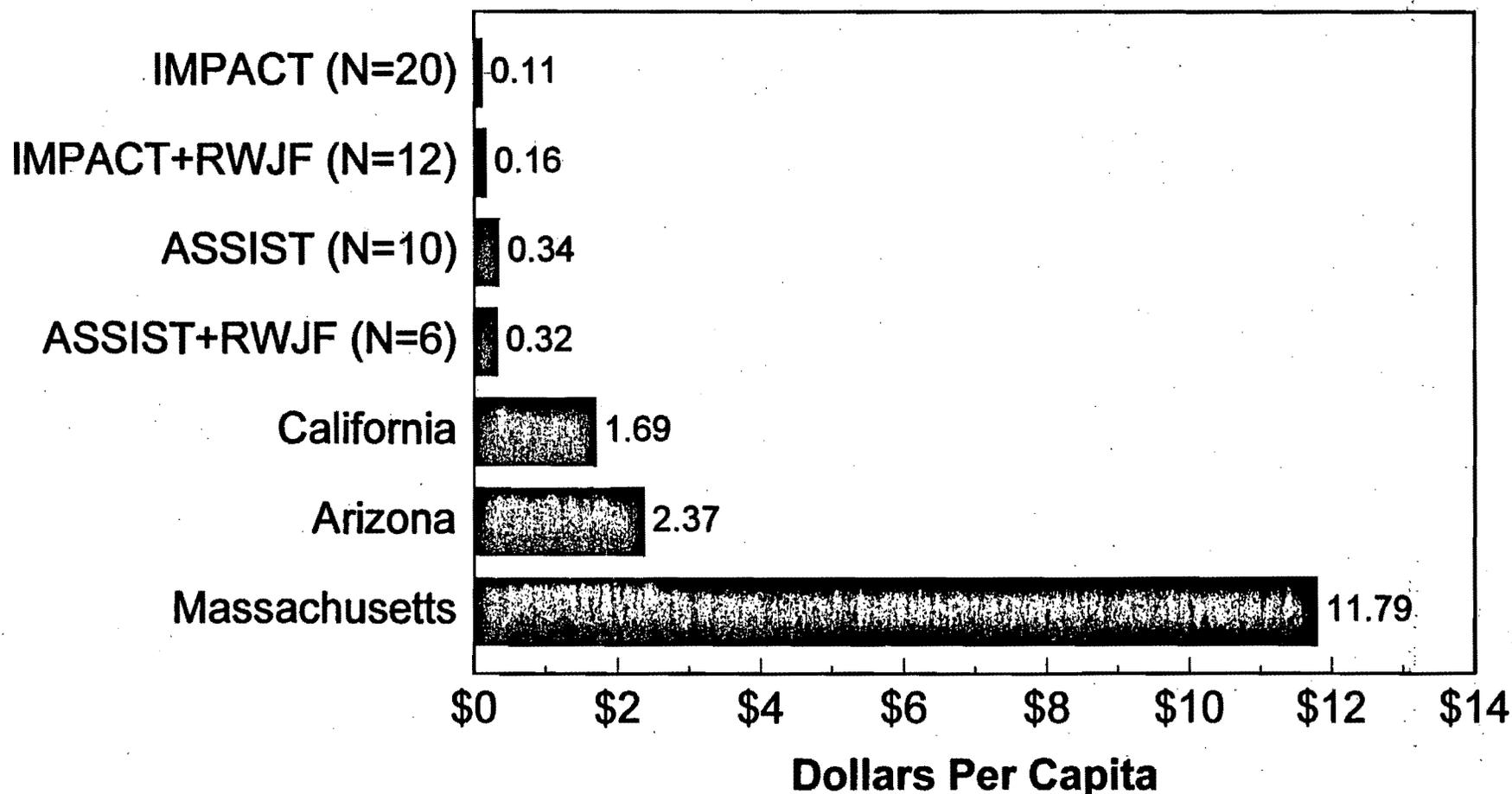
- Utilization data on OTC patch and gum suggest a more than doubling in utilization due to OTC availability of NRT (Walsh American 1995; Nielsen 1996).
- It has been estimated that with the OTC gum and patch, 175,000 to 350,000 additional smokers will quit each year (Walsh America 1995; Nielsen 1996).

- Utilization of the Committed Quitters program (free tailored message program available to all purchasers of Nicorette and Nicoderm CQ) has been modest (less than 10% of purchasers)
- A randomized trial conducted by SmithKline Beecham on the Committed Quitters program demonstrated a significant boost in efficacy over use of Nicorette alone (36% v. 24% 28-day cessation at 6 weeks). (Shiffman, unpublished and confidential data)

How can smoking cessation interventions be institutionalized?

- Broad dissemination and adoption of the AHCPR smoking cessation guideline
- Establishment of tobacco use as a vital sign (asked at every visit)
- Provision of brief advice to quit to all tobacco users and referrals for more intensive services for individuals who express an interest in accessing such services
- Establishment of office systems to support assessing tobacco as a vital sign, providing brief advice to quit, and following up with referrals for more intensive services
- Broader access to (and reimbursement for) effective treatment
- For Medicaid, inclusion of cessation in managed care and other contracts
- For Medicare, coverage of smoking cessation intervention, including NRT
- Accountability within the health care system for aggressive cessation efforts, e.g., stronger requirements from HEDIS and other managed care report card systems
- Proper measurement of the performance of institutionalized cessation efforts based on penetration of the smoker population and reductions in prevalence, not simply whether coverage or a program exists.

Per Capita Spending on Tobacco Prevention and Control -- FY1995



*Proposed Spending for FY97

DRAFT (July 9, 1997)

SMOKING CESSATION & EDUCATION
Workgroup Consensus: Highlights

Scope of the Problem:

- ▶ There are approximately 50 million smokers, and about 20 million would like to quit. The settlement provides substantial funds to help them do so.
- ▶ There is a direct relationship between cessation of tobacco use and public education, therefore, public education will be treated as an integral component of any approaches designed to reduce the use of tobacco products.
- ▶ Cessation and education strategies must take into account that smoking is an addiction, therefore, it should not be anticipated that success rates for cessation treatments will be comparable to those for more acute processes such as antibiotics for infections. Instead, cessation programs should be regarded in the same light as other chronic conditions such as diabetes, and their success should be held to similar standards.

Settlement Funds Available: In addition to funds specified for cessation and education activities, we should consider crossover with other funding streams, i.e., "Teams' Fund" (\$1.8 billion), and Public Health Trust Fund (\$25 billion):

Funding Mechanisms/Decisionmaking:

- ▶ Mechanisms of administration of settlement funds (e.g., government versus nonprofit entity versus combination of different mechanisms separating control to different pots of money as an accountability feature).
- ▶ Need for investment, decisionmaking and priority-setting mechanisms.
- ▶ Federal programs (NIH ASSIST, CDC IMPACT, ungirded by the funded state and local programs (including school-based programs) can provide infrastructure for new activities--broader program implementation, permitting local control and input, tailored to local needs. Need to look at states that spend more per capita and have more effective programs (e.g., California and Massachusetts).
- ▶ Tribes - the settlement treats tribes like states, but the formula is based on tribal population as a percentage of state population, thus not providing adequate funds for successful program implementation.

Spending Priorities:

- ▶ A lot is known about education and cessation program effectiveness (see attachments). There is an issue about whether to use funds to invest in areas (education and assistance) that create demand for cessation services/products or on service delivery or programs that are or could/should be provided by others (particularly the private sector). In areas where we do fund services, those services should be targeted on certain subpopulations.
- ▶ Need to develop effective cessation programs for youth (controversial, e.g., use of nicotine replacement products).

- ▶ Some portion of cessation and education money needs to go to teach clinicians (nurses and doctors) and managed care plans as to how to encourage smoking cessation.
- ▶ There is some evidence that although it costs more to provide cessation services to more individuals, after a certain point there is an economy of scale, and costs per individual begin to decrease so that the overall program is more cost-effective (i.e., the higher the investment, the more return you probably will see per dollar invested).

Research Needs: Necessary crossover with Settlement's research funding.

- ▶ Need for market analysis for private sector delivery of cessation programs/products--government does not necessarily need to supplant current market demand. In addition, need analysis of insurance plan cessation programs, reimbursement, incentives. Currently, all insurance companies have some sort of limit on cessation programs (e.g., in the form of co-pays and/or limits on the number of visits).
- ▶ Need to characterize why it is so hard to get people into intensive treatment (lack of access when they are ready? too complicated to enter the system?).
- ▶ Need market research on nicotine replacement market (one company spends \$120 M on PR alone for product, profits must be much higher). Specific concern that minorities and lower-income people cannot afford these techniques.

MEMORANDUM

TO: BRUCE REED, ELENA KAGAN

CC: CHRIS JENNINGS, ELIZABETH DRYE, JERRY MANDE, SARAH BIANCHI

FROM: TOM FREEDMAN, MARY L. SMITH

RE: TOBACCO BILLS

DATE: JULY 12, 1997

SUMMARY

This is a follow up to the previous memorandum dated July 9, 1997, that compiled tobacco bills from the 104th Congress and 105th Congress. Below is a more detailed description of various bills.

I. BILLS REGARDING FARMERS

1. **S. 598 by Sen. Bradley (D-NJ) on 3-22-95 (one cosponsor, Sen. Lautenberg (D-NJ)). TOBACCO CONSUMPTION REDUCTION AND HEALTH IMPROVEMENT ACT OF 1995.** This bill amends Section 5701 of the Internal Revenue Code to increase taxes on cigarettes from \$12 per thousand to \$62 per thousand. It also increases taxes on cigars, cigarette papers, smokeless tobacco, and other tobacco products. This act would also impose taxes on tobacco products entering into the United States from a foreign trade zone. This bill also creates a "Tobacco Conversion Trust Fund" by amending Subchapter A of Chapter 98 of the Internal Revenue Code of 1986. The bill would transfer 3 percent of the net increase in revenues received by the increase in tobacco taxes to the trust fund. The funds would then be available to the Secretary of Agriculture for the following purposes:

- (1) providing assistance to farmers in converting from tobacco to other crops and improving the access of such farmers to markets for other crops; and
- (2) providing grants or loans to communities, and persons involved in the production or manufacture of tobacco or tobacco products, to support economic diversification plans that provide economic alternatives to tobacco to such communities and persons.

The bill provides that the "assistance" provided to farmers could include government purchase of tobacco allotments for purposes of retiring such allotments.

2. **S. 804 by Sen. Bradley (D-NJ) on 5-15-95 (no cosponsors). TOBACCO CONSUMPTION REDUCTION AND HEALTH IMPROVEMENT ACT OF 1995.** This bill is virtually identical S. 598 also introduced by Sen. Bradley.

II. BILLS REGARDING THE TAX DEDUCTIBILITY OF ADVERTISING

1. **H.R. 1323 by Rep. McHale (D-PA) on 4-15-97 (34 co-sponsors). TOBACCO ADVERTISING REFORM ACT.** This legislation amends Part IX of subchapter B of Chapter 1 of the Internal Revenue Code of 1986 which adds a section stating: "No deduction shall be allowed under this chapter for expenses for advertising cigars, cigarettes, smokeless tobacco, pipe tobacco, or any similar product."

2. **H.R. 2962 by Rep. McHale (D-PA) on 2-06-96 (22 co-sponsors).** This bill is identical to H.R. 1323 also introduced by Rep. McHale in the 105th Congress.

3. **S. 596 by Sen. Harkin (D-IA) on 3-22-95.** This bill is essentially identical to the two bills listed above.

III. BILL ON ADVERTISING AIMED AT YOUTHS

1. **H.R. 762 by Rep. Hansen (R-UT) on 2-13-97 (5 cosponsors). YOUTH PROTECTION FROM TOBACCO ADDICTION ACT OF 1997.** This legislation bans all advertising of tobacco products. It also prohibits the distribution of any free tobacco product, the sponsorship of any event in a brand name, the marketing of nontobacco products bearing a brand name, and the payment for any tobacco product or brand name to appear in movies, television, and other media or on any toy. This bill prescribes that advertising on tobacco product packages shall be in black and white and shall contain no human figures. Civil actions for injunctions for violations of this Act may be brought in district court.

IV. BILL ON WARNING LABELS

1. **S.527 by Sen. Lautenberg on 4-08-97 (5 cosponsors). TOBACCO DISCLOSURE AND WARNING ACT OF 1997.** This bill makes it unlawful to manufacture for sale any cigarette unless the package contains one of the following warnings:

WARNING: Cigarettes Kill

WARNING: Cigarettes Cause Lung Cancer and Emphysema

WARNING: Cigarettes Cause Infant Death

WARNING: Cigarettes Cause Heart Attacks and Stroke

WARNING: Cigarettes Are Addictive

WARNING: Nicotine Is An Addictive Drug

WARNING: Cigarette Smoking Harms Athletic Performance

WARNING: Smoking During Pregnancy Can Harm Your Baby

WARNING: Cigarette Smoke Is Harmful to Children

WARNING: Smoke from [brand name] Cigarettes Can Cause Cancer in
Nonsmokers

- This legislation also requires labels or other tobacco products which are similar to the labels above. The labels must be placed in the two most prominent sides of the product package and be in a size not less than 33% of the side on which the label is placed. The bill requires the labels to be in black and white.
- This bill also requires a package insert detailing the substances posing a risk to HEALTH contained in the cigarettes.
- Manufacturers also must submit to the Government an annual report listing the nicotine, tar, and carbon monoxide intake for the average consumer.
- The Secretary will also establish a toll-free telephone number and a site on the Internet which shall make available additional information on the ingredients of cigarettes.
- The bill provides that any interested organization may seek to enjoin violations of the act in federal district court.

V. BILL ON PERFORMANCE STANDARDS

1. S. 828 by Senator Durbin (D-IL) on 6-03-97 (2 cosponsors). NO TOBACCO FOR KIDS ACT.

- Within one year after enactment, the Secretary of HHS will conduct a survey to determine the number of children who used each manufacturer's tobacco products within the previous 30 days.
- Manufacturers will face penalties if they do not reduce the number of children who use tobacco products by either a de minimis level (one-half percent of the current number of youth smokers) or by the following percentages:

S.828

Compare to settlement

Year 1: no standard; baseline survey is taken	
Year 2: 20% reduction from baseline	
Year 3: 40% reduction from baseline	
Year 4: 60% reduction from baseline	
Year 5: 80% reduction from baseline	Years 5-6: 30% reduction
Year 6: 90% reduction from baseline	
Subsequent years: 90% reduction from baseline	Years 7-9: 50% reduction
	Year 10 (and after): 60% reduction

- Under the Senate bill, if a manufacturer violates the performance standard, the manufacturer must pay a noncompliance fee of \$1 per pack on all its tobacco sales in the subsequent year (not simply sales to youths). If a manufacturer violates the performance standard for two or more consecutive years, the noncompliance fee is increased by \$1 for each consecutive year of violation. If the manufacturer is within 10% of the required reduction for a particular year, the noncompliance fee will be reduced on a pro rata basis. **Under the settlement:** There is a surcharge of \$80 million for each percentage point

difference between the required percentage reduction applicable to a given year and the percentage by which the incidence of underage use of cigarette products for that year is less than the base incidence percentage. (This amount reflects an approximation of the present value of the profit the cigarette industry would earn over the life of underage smokers in excess of the required reduction). The surcharge may not exceed \$2 billion in any year (as adjusted for inflation).

- Under the Senate bill, the first \$1 billion of noncompliance fees will fund enforcement and public education to discourage children from using tobacco products. Any additional fees will go the Treasury for deficit reduction. **Under the settlement:** 90% of the surcharge goes to state and local government to youth tobacco use.

VI. TOBACCO STATE MEMBER BILLS

1. **S.201 by Senator Ford (D-KY) on 1-23-97 (no cosponsors). TOBACCO PRODUCTS CONTROL ACT OF 1997.** This bill imposes limits on advertisements on billboards within 500 feet of any school; bans advertisements in magazines and newspapers if persons under the age of 18 constitute more than 15% of the total subscribership; prohibits ads in taxis, buses, trains, or in stations unless it is where cigarettes are sold; and bans the use of cigarettes in movies for a fee.

This legislation also amends Section 1926 of the Public HEALTH Service Act (42 U.S.C. sec. 300x-26) to provide that the Secretary may make a grant to a state only if the state makes it unlawful, among other things, (1) to sell tobacco products to anyone under the age of 18 and to sell without verifying the age in face-to-face transactions; and (2) to operate a vending machine unless it is in plain view.

2. **H.R. 516 by Rep. Baesler (D-KY) on 2-04-97 (no cosponsors). YOUTH SMOKING PREVENTION ACT OF 1997.** This bill establishes the federal authority to regulate the sale, distribution, and advertising and promotion of tobacco and other products containing nicotine as a condition to the receipt by states of the Federal Preventive Health and Health Services Block Grant. Under the bill, the Secretary may only make a grant under section 1921 of the Public Health Service Act if the State has a law, that among other things, prohibits the sale of nicotine to minors; prohibits the purchase by minors; requires the posting of signs stating the minimum purchase age; requires retail employers to notify its employees about the laws regarding sales to minors; requires retail employees to sign forms that they have received notice; and requires the licensing of retail sellers of nicotine products.

3. **H.R. 2414 by Rep. Baesler (D-KY) on 9-28-95 (3 cosponsors): YOUTH SMOKING PREVENTION ACT OF 1995.** This bill is identical to H.R. 516 introduced by Rep. Baesler in the 105th Congress.

4. **H.R. 2653 by Rep. Charlie Rose (D-NC) on 2-06-96. TOBACCO AMENDMENTS ACT OF 1995.** The main sections of the Act are the following:

- Sec. 2. Elimination of Federal Budgetary outlays for tobacco programs.
- Sec. 3. Establishment of farm yield for flue-cured tobacco based on individual farm production history.
- Sec. 4. Removal of farm reconstitution exception for burley tobacco.
- Sec. 6. Expansion of types of tobacco subject to no net cost assessment.
- Sec. 7. Repeal of reporting requirements relating to the export of tobacco.
- Sec. 8. Repeal of limitation on reducing national marketing quota for flue-cured and burley tobacco.

5. **S. 1262 by Sen. Ford (D-KY) on 9-20-95. TOBACCO PRODUCT CONTROL ACT OF 1995.** This bill is basically an earlier version of S.201 introduced by Sen. Ford on 1-23-97, which is described above.

VII. BILL REGARDING MEDICAID BY REP. OBERSTAR

1. **H.R. 3779 by Rep. Oberstar (D-MN) on 7-10-96 (16 cosponsors): TOBACCO MEDICAID RECOVERY ACT OF 1996.** The purpose of this bill is to reward states that successfully recover the federal and state health care costs incurred under the Medicaid program for the treatment of individuals with diseases attributable to the use of tobacco products by providing increased funding for their Medicaid programs and to provide increased resources to the National Institute of Health. Section 1903(D) of the Social Security Act is amended to provide that if a state recovers amounts expended as medical assistance for the treatment of diseases attributable to tobacco, the Secretary shall determine the amount of federal expenditures attributable to the amounts recovered, based on the federal medical assistance percentage. The Secretary then will treat this amount as an overpayment and permit the state to retain one-third of such amount for the purpose of using the funds to meet the non-federal share of expenditures under the state plan and pay one-third of such amount to NIH.

VIII. BILL REGARDING NICOTINE ADDICTION BY REP. MEEHAN

1. **H.R. 1853 by Rep. Meehan (D-MA) on 6-15-95 (9 cosponsors): FREEDOM FROM NICOTINE ADDICTION ACT OF 1995.** This bill amends the FDCA to make it illegal to introduce into interstate commerce any tobacco product that contains nicotine in the following amounts per cigarette:

As of January 1, 1997	10.00 MG. Nicotine.
As of January 1, 1998	8.00 MG. Nicotine.
As of January 1, 1999	6.00 MG. Nicotine.
As of January 1, 2000	4.00 MG. Nicotine.
As of January 1, 2001	2.00 MG. Nicotine.
As of January 1, 2002	.05 MG. Nicotine.