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Title: **THE EMERGING MARKET FOR LONG-TERM NICOTINE MAINTENANCE**

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ABSTRACT

In increasing numbers, Americans will seek to satisfy nicotine addictions through the use of novel nicotine-delivery products devoid of the tar and carbon monoxide that make cigarettes so deadly. In the vanguard are tobacco industry devices that heat rather than burn tobacco and pharmaceutical industry nicotine-replacement products, with nicotine "gum" and the patch now available over the counter. Ostensibly, these two industries have diametrically opposed objectives, the tobacco industry striving to sustain nicotine addictions, the pharmaceutical industry to end them. However, a series of technological, economic, political, regulatory, and social developments augurs a strange-bedfellows competition in which these industries will vie for shares of a new multibillion dollar long-term nicotine maintenance market. Regulatory options range from encouraging competition to banning all nicotine-delivery devices. A more realistic approach discourages use of the most dangerous products, while making relatively nonhazardous products readily available to adults.

Accounting for a fifth of all deaths in America,[1] the toll of tobacco is all too familiar. So, too, is the ultimate source of tobacco's toxicity: the extraordinary grip that nicotine places on its users.[2]

As with other addictions,[3,4] becoming abstinent from nicotine is definitely possible; half of currently alive Americans who have ever smoked have quit, usually without clinical assistance. However, for many of the millions who remain smokers, most of whom say that they want to stop, efforts to quit have failed, often despite frequent attempts.[5]

Recognition of the tenacity of their smoking and its eventual deleterious consequences has led some health professionals to question continued, complete reliance on the traditional treatment paradigm, which has regarded abstinence as the only therapeutic goal. Instead, they are cautiously considering a harm reduction strategy that envisions a role for long-term nicotine maintenance using products that deliver nicotine without the other toxic substances in tobacco products.[6-10]

At the heart of the nicotine maintenance concept lies the belief that, although it is not risk-free,[11-14] nicotine *per se* does not directly cause most of the enormous burden of tobacco-related disease. Rather, it is the tobacco products themselves (and their combustion products), the vehicles that deliver nicotine, that are "dirty" and dangerous.

The avoidance of tobacco use is thus considered far more important than kicking an addiction to nicotine. For those who cannot or will not stop using nicotine, might it not be prudent to offer an alternative to tobacco products, one that satisfies their addiction while dramatically reducing their risk of disease?

This question is actually quite complicated, requiring resolution of a myriad of issues.

Can consumer-acceptable products be developed that will satisfy nicotine needs without subjecting consumers to substantial health risks? (What constitutes "substantial"?) Would such products induce children who do not now use tobacco products to initiate nicotine addictions? Would they cause former smokers to relapse? To what effect? (What is the abuse potential of such products?) Would users of such products also use conventional tobacco products? Would the availability of alternative nicotine delivery devices substantially reduce the numbers of people who successfully become abstinent in the future? Again, to what effect? (Again, what is "substantial"?) How would the nation's drug regulatory apparatus respond? Under what circumstances would the sale of such products be permitted?

These are not merely abstract questions. A series of technological, economic, political, regulatory, and social developments has brought us to the brink of a new market for long-term nicotine maintenance. Whether or not the health community finds this desirable, these developments mean that tobacco users -- and possibly nonusers -- are likely to have growing numbers of nicotine-maintenance options available to them soon. Some will involve no tobacco; others will use tobacco in ways not previously imagined. There are scores of patents for such devices, including an electrically-fired pseudo-cigarette.[15]

The options that will eventually be brought to market and the conditions of their availability remain to be defined. It is here that the health community can work with the larger society and its formal policy-making apparatus to shape the future of long-term nicotine maintenance. To broaden the debate, we describe developments that are forcing the issue and consider alternative approaches to defining and regulating a future market for nicotine-maintenance products, including those that use tobacco derivatives as the vehicle for

delivering nicotine and those that do not. We derive salient lessons for the emerging environment of nicotine delivery from the history of innovation in the cigarette industry.

RECENT AND ANTICIPATED DEVELOPMENTS

New technology for delivering nicotine is evolving rapidly and dramatically. Some of the technology already commercially available is very familiar, such as two nicotine replacement therapy (NRT) products: "gum" (nicotine polacrilex) and the patch.[16,17] Some new technology has been introduced but is less familiar, including two cigarette-like devices from the R. J. Reynolds Tobacco Company, Premier and Eclipse.[18-20] Finally, some of the new nicotine-delivery technology is quite unfamiliar. For example, nicotine nasal spray became available as a prescription drug in 1996 and Food and Drug Administration approval of a nicotine inhaler has recently been recommended by a federal scientific advisory panel.[21,22]

All such products emerge in response to market conditions and the social, regulatory, and political considerations that define them. As discussed below, the cigarette manufacturers' introduction of products like Eclipse represents a marketing response to a social environment increasingly hostile towards environmental tobacco smoke and to a marketplace of health-concerned tobacco consumers. Unlike NRT products, which also represent a response to consumer health concerns, Eclipse is not intended as a bridge to abstinence. Also unlike NRT products, the manufacturer has not submitted Eclipse to the FDA for evaluation of safety and determination of marketing conditions.

In terms of their purposes, new products from the cigarette companies and nicotine

replacement pharmaceuticals appear to be worlds apart, the former dedicated to the perpetuation of nicotine dependence, the latter to its curtailment. However, plausible developments in both product categories and in the conditions of their availability could well make the cigarette and pharmaceutical companies the strangest of bedfellows, competing vigorously for a large market of long-term nicotine maintainers. The logic underlying this statement will emerge following consideration of each industry's innovations.

New-generation cigarette-like devices, and old-generation effects on health

Eclipse might appear to represent a radical and even revolutionary change in both industry product and approach. As we discuss below, however, Eclipse follows a tradition of industry response to threats to sales posed by consumer concerns about the conventional product.

Structurally, Eclipse is dramatically different from the conventional cigarette, especially since it burns very little tobacco-like material. A carbon fuel element, insulated with a fiberglass jacket, heats a glycerin-laden charge of reconstituted tobacco. This vaporizes material that cools to condense into an aerosol largely made up of water and glycerin droplets that, in turn, carry nicotine and other volatiles. The consumer inhales an aerosol consisting largely of water, glycerin, nicotine, and the oxides of carbon. Nicotine is delivered at about the same rate and amount as a cigarette having an FTC rated yield of 0.9 mg. Carbon monoxide is moderately higher than that delivered by such a cigarette.[19,20,23,24]

Eclipse is being test-marketed in Chattanooga, Germany (under the name HI-Q), Sweden (Inside), and Japan (AIRS). The only similar device was its immediate predecessor,

Premier, a more radical innovation that produced an aerosol from glycerin and a tobacco extract adsorbed onto alumina beads just proximal to the carbon fuel element. Introduced in 1988, Premier failed market tests and was taken off the market amid mounting pressure on the FDA to regulate it under the Food, Drug and Cosmetic Act.[25]

Both Premier and Eclipse seem designed to address two industry problems: smokers' concerns about the health effects of smoking, specifically its carcinogenic potential (aerosols from both products contain low levels of carcinogens compared to conventional cigarettes), and nonsmokers' concerns about environmental tobacco smoke (ETS) (neither product produces much visible smoke). The latter has implications for the social acceptability of such products and quite possibility their legal acceptability. Would workplace policies and public regulations be modified to permit consumers to use such reduced-smoke devices in places where smoking is banned?

Both of these industry problems have been addressed, largely without success, by earlier generations of product innovation. The ETS issue is of more recent vintage, and relevant innovations are fewer in number. Two were cigarettes with a built-in perfume and low-smoke cigarettes, designed with special papers resulting in less visible sidestream particulate matter.[26,27]

Health concerns drove the two major previous paradigm shifts in cigarette architecture: filter-tipped cigarettes in the 1950s and low tar and nicotine cigarettes at the end of the following decade, both presented to the public as radical design changes, much like the emerging generation of devices.

Filters were the industry's response to the then newly emerging public concern about

smoking's relation to lung cancer.[28] The cigarette companies marketed filters as trapping the dangerous components of cigarette smoke but letting the "flavor" through, although filters never received independent reviews confirming the claims.[26] Affording smokers an apparent alternative to quitting smoking, filters quickly became the dominant product on the market. Their introduction and effective marketing reversed a two-year decline in per capita cigarette consumption in 1953 and 1954 that had resulted from new evidence linking lung cancer to smoking, which then meant unfiltered cigarettes.[25] Ironically, the most successful early filter, touted quite explicitly for its health protection properties, the Kent Micronite filter, used crocidolite asbestos as the filtering agent.[29,30] That filters were introduced primarily as a public relations gambit, rather than as a truly less dangerous product, is suggested by the fact that some early filtered cigarettes used harsher tobaccos, so that the filtered smoke would taste like the unfiltered smoke of old.[28]

The 1964 Surgeon General's report[31] began a process that led to the industry's next technological "fix": low tar and nicotine (t/n) cigarettes, marketed, often explicitly, with the theme that health-conscious smokers had the choice of either quitting smoking or switching to low t/n brands.[32] By 1981, low t/n cigarettes had captured a majority of the market. Medical textbooks frequently recommended their use by patients unable or unwilling to stop smoking.[33,34]

Since then, scientists have learned that smokers who switch from regular cigarettes to low t/n brands engage in "nicotine regulation," compensatory behaviorial changes that greatly narrow the supposed gap between high and low yielding cigarettes. Low t/n smokers may consume more cigarettes, take larger and more frequent puffs, inhale more deeply, smoke to

a shorter butt length, and subvert the technologies that lower machine-measured t/n yields (by blocking ventilation holes in filters that, unoccluded, dilute smoke by mixing it with air).[2,35,36]

The net effect is that, consistent with smoking being a drug dependence process, the variance in smokers' blood cotinine levels is significantly smaller than the variance of nicotine deliveries indicated in cigarette ads.[37] The public is unaware that t/n ratings are derived from standardized machine smoking of cigarettes, in which cigarettes are puffed at a constant volume (35 ml) and at a constant interval (60 seconds). As the data on nicotine regulation demonstrate, people do not usually smoke like the machines.[38]

Low t/n cigarettes would likely reduce health risks if smokers did not engage in nicotine regulation to a significant degree and if they would have continued to smoke even if low t/n cigarettes were not on the market. However, most smokers who "switch down" to low t/n cigarettes do engage in nicotine regulation.[35,36,39] Further, logic, available survey and marketing data, and internal tobacco company documents suggest that the availability of low t/n cigarettes substantially impeded smoking cessation.[25,40-43] On balance, therefore, low t/n cigarettes may well have *increased* the aggregate societal burden of smoking, primarily by reducing the number of people who would have quit in the absence of their availability, and secondarily by switchers smoking more cigarettes.[25]

A similar phenomenon undoubtedly characterized the success of filtered cigarettes in reversing the decline in cigarette consumption in 1953-54. In both instances, a major technological innovation, marketed as promising reduced harm from smoking, may well have had the opposite effect in the population as a whole. Cigarette use likely would be much

lower today if the only products for sale were 70 mm unfiltered smokes. The introduction and diffusion of these new types of cigarettes thus clearly benefitted the industry by maintaining or increasing sales. Industry documents show that industry scientists regarded low-tar cigarettes as "health-image" products, public relations gimmicks, rather than truly "health-oriented" products.[41]

The introduction of Eclipse thus follows a decades-old tradition of industry product innovation in response to public concern, with the industry's intent being to reduce concern and thereby maintain or expand sales. More similarly motivated new-generation products will likely soon appear, especially if Eclipse is successfully introduced.[15,19] Whether past history is relevant to the new generation products remains to be seen. The promise of reduced risk for confirmed smokers may be genuine this time, especially with regard to cancer. If history repeats itself, however, this ostensibly less-hazardous product might sustain high levels of nicotine addiction and, on balance, increase the aggregate disease toll.

One great risk specific to low-smoke devices is that they may be deemed acceptable for use in settings in which smoking is prohibited, such as workplaces. A plausible consequence would be regular cigarette smokers' consuming these devices during work hours, when at present they do not smoke, and then continuing to smoke their regular brands outside of work. The net effect would be increased exposure to nicotine and carbon monoxide, since workplace smoking bans decrease daily cigarette consumption.[44] For people who would have quit smoking in the absence of the day-time nicotine alternative, all of the risks associated with smoking would be greatly increased.

Nicotine-containing pharmaceuticals

The advent of NRT pharmaceuticals revolutionized the treatment of nicotine dependence, in part by medicalizing it. Prior to their availability, the clinical armamentarium was limited primarily to behavioral counseling, which, for a variety of reasons, held little appeal for either physicians or patients.[45] Although a few smoking-cessation products were available in the commercial market, none had demonstrated efficacy in controlled trials.[25,46] Tests of both nicotine polacrilex ("gum") and patches as adjuncts to behavioral counseling demonstrated efficacy, on average doubling quit rates.[16] NRT products thus afforded physicians the opportunity to prescribe something potentially efficacious for patients who wanted to quit smoking, thereby making the physician-patient interaction more conventional and comfortable for both parties.

Nicotine gum introduced the era of NRT pharmaceuticals in the United States in 1984, followed by patches in 1991 and nicotine nasal spray last year, with the nicotine inhaler on the horizon. A nicotine-containing lozenge on a stick (like a lollypop)is also being developed.[47] Each of these newer products has its own set of attractive features and limitations, the latter including abuse potential and other adverse side effects. Each product holds the promise of helping an as-yet undefined subset of smokers. Researchers are investigating combination therapies as well, attempting to exploit the specific virtues of the different products.[48]

As important as the development of NRT products may be a major change in product distribution: over-the-counter (OTC) sale, of gum and patch thus far. Although the quit rate will be lower than that associated with using NRT under the guidance of experienced

clinicians, greater NRT accessibility could more than compensate, leading to more quitting in the aggregate.[49]

OTC availability will also likely increase the use of nicotine-bearing products as partial or complete *ongoing* substitutes for cigarette smoking (and other tobacco-product use). It will likely routinize the use of NRT products by smokers not trying to quit, to supply nicotine when they are not smoking, either because they want to reduce their cigarette consumption or because law or custom precludes their smoking in certain locations (e.g., workplaces or airplanes).[10,50] For this use, NRT products should logically be called nicotine *maintenance* products.

Strange bedfellows

Through product innovation by tobacco companies, pharmaceutical companies, and other consumer products companies, and through OTC distribution of NRT products, the lines distinguishing different types of new-generation nicotine delivery devices could eventually become blurred. More or less intentionally, each company could find itself maintaining nicotine dependence among consumers whose choices would otherwise be limited to conventional tobacco products or abstinence. Ironically, tobacco companies and pharmaceutical companies, which approach nicotine addiction from diametrically opposite positions, could find themselves in direct competition for sales of nicotine maintenance products among the same group of consumers.

In this regard, the history of tobacco company innovation, described above, is not encouraging: previous generations of ostensibly "less hazardous" products may well have

increased the harm caused by cigarettes, by encouraging the maintenance of smoking rather than quitting. Still, some future tobacco industry product may overcome enough of smoking's dangers that the cost of substitution of this product for cigarettes -- continued dependence on nicotine -- will fall short of the benefit of reduced aggregate exposure to the other poisons in cigarette smoke.

There is insufficient history of pharmaceutical industry activity in this arena to draw direct historical lessons. However, with a potential market in the tens of millions of consumers in the U.S. alone, the pharmaceutical industry would have to seriously consider aggressive involvement in a reconceptualized nicotine maintenance market. Drug companies are competing with advertising campaigns for OTC gum and patch exceeding $100 million, which would certainly pay off more handsomely if consumers used these products over a long period of time.[51,52] The relative ease of the transition from focusing exclusively on nicotine replacement to contemplating a much larger market for nicotine maintenance has been hinted at in ads promoting a non-nicotine smoking cessation aid, CigArrest, "for those times when you want to stop smoking, *for a moment* or forever" (emphasis added).

ALTERNATIVE SCENARIOS FOR THE FUTURE AVAILABILITY OF NICOTINE

For many health professionals, contemplating competition between the tobacco and pharmaceutical industries for long-term nicotine users will generate a sense of moral repugnance. Like it or not, however, this competition is developing and will continue to develop, barring extraordinary regulatory measures (e.g., the FDA's returning gum and patch to a prescription-only distribution and prohibiting the marketing of any new tobacco

industry products not demonstrated to be safe).

An optimal set of market and regulatory circumstances could conceivably create incentives that encourage the development of truly much less hazardous methods of consuming nicotine. Note that we have had a market for long-term nicotine maintenance for decades: the tobacco market. Through strict regulation of nicotine in nontobacco products, and virtually no regulation of tobacco products, we have, essentially, granted the tobacco industry a monopoly in the nicotine maintenance market. This market has been accompanied by an unprecedented burden of disease and death. Reconceptualizing that market, opening it to innovative, less hazardous products introduced through competition between the tobacco and pharmaceutical industries, could conceivably satisfy the public's desire for nicotine without exacting the current enormous cost in ruined lives.

The creation and marketing of novel nicotine delivery devices raise a myriad of possible scenarios concerning the future availability and use of both tobacco and non-tobacco nicotine-bearing products. Here we summarize scenarios defined by the regulatory approach adopted. Product availability and use will also be defined by consumer demand. Without discussing this explicitly hereafter, we assume that many consumers will want to use nicotine devices characterized by convenience, reasonable price, social acceptability, and provision of a high degree of nicotine satisfaction.

Either consistently or idiosyncratically, each of the product categories -- current tobacco products, new tobacco industry nicotine delivery systems, and nicotine devices produced by the pharmaceutical or other industries -- could be regulated according to the following options: (1) no regulation; (2) legal availability on a nonprescription basis; (3)

availability by prescription only; (4) not legally available. In addition, regulation could include limits on advertising, disclosure of information to consumers, and so on.

Conventional tobacco products are currently subject to no health and safety regulation. In contrast, all pharmaceutical company innovations have been submitted to and regulated by the FDA, with efficacious nicotine replacement products first permitted for prescription sale and then OTC, if their abuse liability is deemed low. The FDA has also asserted its authority over other nicotine delivery devices not submitted to the agency for approval. Favor, a precursor to the new inhaler, was prohibited as an untested drug delivery system. Similarly, the FDA determined that Masterpiece Tobacs, a chewing gum containing shredded tobacco leaf intended for use "Anytime, when you can't smoke," was a food product adulterated with an unapproved additive, tobacco.[25]

The regulatory status quo is thus well defined, with one critical exception: innovative tobacco industry products. To date, no tobacco company has submitted an innovation for FDA approval, and the agency has not asserted its regulatory authority when confronted with a product from a major producer. However, the FDA has been petitioned to regulate Eclipse.[53] The agency was considering claiming regulatory jurisdiction over Premier before R. J. Reynolds removed it from the market.[25]

A future regulatory structure for nicotine delivery devices could continue current policy, with new tobacco industry products either treated like conventional tobacco products or like conventional pharmaceutical products. Alternatively, it could treat all nicotine-yielding products identically, regulating them as either prescription or nonprescription drug delivery devices. In theory, a decision could be reached to keep government out of the

nicotine market altogether, allowing a free enterprise shoot-out between the tobacco and pharmaceutical giants. As unlikely as that seems, another possibility -- banning all nicotine-yielding products -- is even less conceivable.

A more rational regulatory approach might be to advantage less toxic products, instead of honoring accidents of history, as at present. All currently available nicotine delivery devices would continue to be sold, but the least toxic would be the most easily available and attractively presented, as discussed below. Such an approach could also provide incentives, or requirements, for incremental improvements in conventional products, for instance by requiring that cigarettes be fire safe.[25]

A more radical differential regulatory strategy would require reduction of the nicotine content of conventional tobacco products over se/veral years to levels unlikely to cause or sustain addiction.[54] This would afford current users ample opportunity to wean themselves off of tobacco products, while simultaneously reducing the ability of tobacco products to addict future generations of children.

All other nicotine-yielding products, regardless of industry of origin, would be evaluated as drug delivery devices by the FDA, permitting on the market only those that met a relative harm standard. The harm theshold might (for example) tolerate nicotine addiction, at levels deemed unlikely to be harmful to human health, but prohibit any other substances known or believed dangerous to health.

Under this policy, de-nicotined tobacco products could be freely sold, despite their delivery of toxic compounds (possibly subject to age restrictions, as at present). If people really smoke for "flavor" or "taste" -- the predominant tobacco industry claim -- sales of

tobacco products should not be impacted. If, in fact, people smoke primarily to satisfy nicotine addictions, few if any consumers likely would choose to use de-nicotined products on a regular or even frequent basis. This appears to have been the experience with Next, a de-nicotined brand introduced by Philip Morris in the late 1980s that failed its market tests.[55]

In addition to determining legal availability, regulatory agencies frequently regulate circumstances of manufacture, marketing, time and location of sale, and age of purchase. FDA regulation of cigarettes and smokeless tobacco, to protect children, focuses exclusively on just such conditions of marketing and sale.[56]

Future nicotine delivery device regulation could rely heavily on differential marketing and sale conditions to reduce the attractiveness of the most hazardous products and increase that of the less hazardous. For example, firms might be permitted to advertise, without restrictions, products that FDA found minimally dangerous. In contrast, if permitted at all, cigarette ads might be limited to black-and-white block-letter factual text. Similar distinctions could be made with regard to packaging, with plain packaging required for the most dangerous products, such as cigarettes, with warning labels consuming a third to a half of the front panel of the package.[57,58] Differential rates of excise taxation might be employed to encourage consumer use of the less hazardous products.

Developing a comprehensive, rational, politically feasible nicotine policy is a challenge of the first order. It ought to begin with a few basic principles. First, conventional tobacco products should be grandfathered in the early-going. For political and social reasons, a phase-in period of years should be established for mandated major changes in conventional products, such as lowering nicotine to nonaddicting levels,[54] with the

assurance that reasonable alternative nicotine delivery devices will be available. There is no reason, however, to delay marketing, packaging, and sales restrictions to reduce the glamorous imagery associated with tobacco use, or incremental product design changes helpful to the public's health (e.g., fire safety).

The second principle should be consistency, to the extent pragmatically possible. If any new nicotine delivery device is subject to FDA approval, all should be treated likewise. Thus, since the new nicotine inhaler requires FDA approval, so should Eclipse. If the FDA deems that the risks associated with the inhaler warrant prescription-only distribution, a similar conclusion about Eclipse should lead to a similar requirement.

The call for consistency reflects the ironic reality that new pharmaceutical products currently face a long and expensive marketing approval process, while the most dangerous nicotine delivery device ever invented, the cigarette, is introduced and sold without regulatory impediments. In essence, the deck of competition has been stacked heavily in favor of conventional tobacco products. An entrepreneur with a tobacco- (but not nicotine-) free product that is unarguably less dangerous than cigarettes, as was Favor, cannot simply take that product to market in an attempt to compete with cigarettes.[25]

The final principle is that the primary goal of a new nicotine policy should remain to help everyone who wishes to be free from nicotine and tobacco to achieve abstinence. For those unable or unwilling to be nicotine-free, the policy should offer alternative means of achieving homeostasis that minimize abuse potential and risks to health.

TOWARD DEVELOPMENT OF A NICOTINE POLICY

The intent of a rational nicotine policy must be to deal realistically and constructively with the public health disaster wrought by the widespread use of tobacco products. An underlying premise, supported by a wealth of evidence, is that, because of addiction, tobacco products exact their toll predominantly involuntarily on the part of consumers. With rare exceptions, nicotine addiction begins during childhood and adolescence; despite sincere desires to quit, many simply find the chore too taxing.

With tens of millions of Americans currently addicted, continued dependence on nicotine for large numbers is a virtual certainty for the foreseeable future. "Large numbers" does not imply that all or even most of today's addicted population will always remain addicted; even a relatively small proportion represents a substantial number of people. Furthermore, a variety of social forces leading new generations of children to become nicotine-dependent will persist during much of that future.

People who are nicotine-dependent are victims of addiction and not social miscreants. They deserve a policy that recognizes their individual dignity, the difficulty many would have in being forced to forgo nicotine, and the opportunity to continue consuming nicotine should they so desire. At the same time, children deserve the opportunity to grow up free of inducements to become addicted to nicotine. As such, the option of having minimally harmful nicotine products available to adults, in a social and policy environment that deglamorizes nicotine consumption, seems worthy of open-minded consideration. To achieve such an environment requires serious restriction of children's access to nicotine products and of the marketing of such products. Assuring adults continued availability of nicotine products acknowledges that significant numbers of Americans will be unable or unwilling to

stop using nicotine.

The notion of nicotine maintenance in less harmful forms, rather than complete abstinence, is not new. Following the introduction of filtered and then low t/n cigarettes, numerous health professionals supported switching from the conventional product to the innovation.[41,59] More recently, an oral pathologist has advocated the use of smokeless tobacco products as a less-dangerous alternative for addicted cigarette smokers.[60]

With hindsight, support of filtered and then low t/n cigarettes appears to have been misguided, quite possibly the cause of more rather than less tobacco-produced disease. Similarly, encouraging addicted smokers to switch to smokeless tobacco products appears short-sighted,[61] especially given the availability of the new NRT devices, the spray and the inhaler. These are far "cleaner" than smokeless tobacco and may satisfy nicotine needs at least as effectively.

The approach considered here, nicotine maintenance for some addicted consumers through the provision of less toxic nicotine delivery devices, has been advocated for quite a while by a handful of prominent scientists.[6,62,63] Nevertheless, nicotine maintenance is certain to be unpopular with many seasoned veterans of the tobacco wars. Acknowledgment of the possibility of a world in which nicotine addiction might be tolerated, and even encouraged, would be a bitter pill to swallow for many health professionals.

Stopping short of supporting a ban on cigarettes, universally recognized as implausible (and we believe undesirable), a prevalent "zero tolerance" philosophy derives in part from the accurate perception that, to date, ostensibly risk-reducing product innovations have typically had quite the opposite effect. For at least some members of the tobacco-

control community, it also likely derives in part from a puritanical streak and a cynicism fed by decades of consistently dishonest and dangerous tobacco industry behavior.[28,41,64] Such people may find completely unacceptable the tobacco industry's continuing to profit from the sale of any kind of product, especially one that perpetuates nicotine dependence.

Adoption of a nicotine maintenance policy is fraught with dangers, as well as opportunities; the two may occur together. For example, to compete successfully with cigarettes and other tobacco products, nicotine-only pharmaceuticals may need to be made more attractive to consumers. The current unappealing flavor of nicotine gum may have to be improved. Similarly, more efficient (rapid) means of getting nicotine into the brain may be required (e.g., the new spray or inhaler). Therein lies the promise of consumer-driven shifts away from tobacco products; but the very process of making nicotine products competitive with tobacco products, from a consumer's perspective, will increase the abuse potential associated with the new products. This amplifies the need to ensure that any involved regulatory authority develops explicit objectives and criteria with both foresight and flexibility. Flexibility may prove essential to deal with failures in the domain of foresight: any regulatory system will need to make adjustments in light of actual experience.

The presence of alternatives to conventional tobacco products will influence the degree to which people seek abstinence, and there may be shifting back and forth among delivery devices. The risks faced by novices, the young, under various scenarios will have to be carefully considered as well. What may be good policy for dealing with the current generation of tobacco users may not be so good for future generations. It would be prudent for a national nicotine policy to be subject to periodic review and revision.

A nicotine maintenance market will emerge from the present ferment in device innovation. However, its precise characteristics remain to be established. We urge the health community, and the broader public as well, to engage in thoughtful research and discussion on the nature of this market and on the characteristics it ought to have. In so doing we should draw on the experiences of numerous countries around the world, in which governments are developing a variety of approaches to manage this market. The stakes are extraordinarily high.

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July 25, 1997 (rev. July 28)

Jerold Mande
Senior Advisor to the Director
Office of Science and Technology Policy
Old Executive Office Building, Room 346
17th Street and Pennsylvania Avenue, NW
Washington, DC 20502

Re: The Final Report of the Advisory Committee on Tobacco Policy and Public Health (the "Koop-Kessler report"), John Slade's July 7 analysis of the Proposed Tobacco Settlement, and July 27 comments from the Society for Research on Nicotine and Tobacco (SRNT).

Dear Jerry:

It is inspiring to see how much work you and others on the White House staff have devoted to ensuring an expedited yet thorough review of tobacco control options, and to see how committed you all are to public health interests. We are now starting to witness growing consensus among many in the public health community regarding the Proposed Tobacco Settlement. Yet a number of us still have different priorities; this is evident in the somewhat differing emphases of the Koop-Kessler report and the comments of SRNT and Dr. Slade. Most importantly, however, these three analyses all stress the importance of keeping the public health at the forefront and solid science as our foundation. All these views deserve careful consideration as we progress in this process of reaching a settlement.

A congressionally and presidentially endorsed Tobacco Settlement would indeed offer basis for rapid and substantial policy changes that could contribute to improved public health. As I've said before, we need to stay focused on public health consequence that lie five or ten, or 50 and even 100 years in the future. While it is certainly important to take accelerated action to reduce the immediate toll of tobacco-related death and disease (through, for instance, improved access to smoking cessation treatment), we need to be mindful of the importance of such long-term investments as a well-supported research infrastructure and youth prevention and treatment efforts. The Proposed Tobacco Settlement provides a fine starting point for negotiating a settlement with a stronger health focus, but certain issues belong at the forefront of our deliberations. Five of them are particularly important:

(1) The FDA Tobacco Rule provides a well-documented and scientifically-based blueprint for our efforts. Its focus lies on the reduction of tobacco-related death and disease—not on the total punitive damages sought from the tobacco industry. We should be more concerned with how funds resulting from this Settlement could be spent to improve the health of Americans

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than with debating whether payments from the industry are sizable enough. Those of us who have helped document the magnitude of unnecessary death and disease caused by the tobacco industry may find that difficult to accept, but trying to secure future public health and at the same time settle on just retribution for past wrongs seems a mighty task. We also need to remember the plight of current tobacco users. Whatever sums are agreed upon, the settlement must ultimately reduce smoking prevalence nationwide, as well as produce drastic changes in the product tobacco companies offer the public, circumscribe tobacco marketing approaches, and improve the likelihood of industry-wide shrinkage. These aims are consistent with those stated in the FDA Tobacco Rule. Although they may not be priorities for those who evaluate the settlement by the degree to which it rapidly and substantially hits industry pocketbooks, it seems quite possible to bankrupt existing tobacco companies (by triggering a myriad of complicating and extended legal action, for example) without improving public health.

(2) Goals for reduced smoking prevalence in the total population are worthy of exploration. For example, a decline of 1% per year over one or two decades seems a reasonable goal. Our experience with other highly toxic and addictive drugs suggests that if we achieve single-digit prevalence, we will face increased difficulty in making further reductions and may need to consider additional tobacco control measures at that time.

(3) Research on tobacco and nicotine must be complementary, supportive and expanded. We have the elements of a research infrastructure, but lack the framework necessary for building an infrastructure that will last into the next century. There is compelling need for research in at least four different areas, if we are to maximize the immediate benefits of scientific findings, minimize the undesirable consequences of ongoing tobacco use and initiation, and embark on a course that produces an increased capacity to reduce tobacco-related death and disease. Four federal agencies—the Agency for Health Care Policy and Research (AHCPR), the Centers for Disease Control and Prevention-Office of Smoking and Health (CDC-OSH), the National Institutes of Health (NIH), and the Food and Drug Administration (FDA)—that already play key roles in coordinating and overseeing such research could be encouraged (and of course, funded) to expand their current work.

a. Surveillance Research (CDC-OSH): Rapid, responsive and much more comprehensive monitoring of the use of all forms of nicotine is needed to provide mid-course policy corrections, to guide regulation, and to enable more rapid dissemination of new treatment approaches.
b. Basic Research (NIH): Research on the pathophysiology and development of nicotine dependence is critical; it provides the basis for improved prevention and treatment efforts.
c. Prevention and treatment research (AHCPR and NIH): We are fortunate that many tobacco-addicted people can be effectively treated along the guideline issued by AHCPR. However, further research in this area must be expanded if we are to act on a course that will take us to continuing reduction of tobacco-caused death and disease. Initial research leading to the development of nicotine patches came out of the National Institute on Drug Abuse (NIDA). NIDA and other national institutes have been helping support the research that has already led to improved efficacy of use

with both the nicotine patch and gum. Such research complements valuable work being done by the pharmaceutical industry.

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

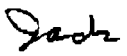
(4) Regulation of all nicotine delivery products must be consistent. There has been much talk of the need for a "level playing field" for nicotine products, be they medications from pharmaceutical companies or cigarettes and snuff from tobacco companies. Our goal should be to undo and reverse the present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

(5) Treatment approaches must become more flexible and readily available. However, as my colleague John Pinney has observed, we need to avoid overstimulating an underdeveloped treatment infrastructure. We also need continued and regular (i.e., annual) reviews of both new and existing treatment processes, work along the lines of an AHCPR review process. Such reviews would undoubtedly be useful to FDA. In addition, we need to improve the acceptability of treatments by devising methods to reach refractory and understudied populations and by allowing for expanded treatment goals. Focusing exclusively on absolute and immediate smoking cessation seems too narrow an approach. Please note that while this suggestion is sometimes misinterpreted as abandoning absolute cessation as the optimal outcome for current smokers, it is not meant to depreciate the value of cessation in any way. Absolute cessation should remain the cornerstone of tobacco control strategies for addicted tobacco users, but it often excludes or alienates tobacco users who are unable or unwilling to presently achieve absolute cessation. No one should be left to unmitigated tobacco use. Experience in other areas of addiction medicine has taught us that there is considerable benefit to broadening treatment strategies and tactics and to include exposure-reduction models.

Clearly, much remains to be done. The Proposed Settlement provides an opportunity to set a nationwide course towards reduced tobacco-caused disease, to the levels of disease caused by the polio-virus, perhaps, or lower. That should be our long-range goal. But substantial progress in achieving that goal will require a comprehensive, iterative process that combines a long-term commitment to progressive research, fair regulation, and generous resources. Several

opportunities lie within our reach in the near future. We should take note of promising initiatives, such as those in California and Massachusetts. What makes them all the more remarkable is that they make inroads in the absence the sort of national supports that now appear possible. These initiatives would benefit considerably from measures that can be most effectively implemented at the federal level, including accurate tobacco labeling, the accelerated development and approval of nicotine-delivering medications, and much more substantial restrictions on tobacco product development, advertising and marketing. Undertaking actions aligned with those described in the FDA Tobacco Rule, the Proposed Tobacco Settlement, and the Koop-Kessler Report holds immediate and long-range promise for health of all Americans.

Sincerely yours,



Jack E. Henningfield, Ph.D.
Vice President, Research and Health Policy
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President Elect,
Society for Research on Nicotine and Tobacco

cc: David Kessler, M.D., J.D.
C. Everett Koop, M.D.
John Seffrin, Ph.D.
The Honorable Donna Shalala
Harold Varmus, M.D.
The Honorable Henry Waxman

enc: Slade comments
SRNT comments (forthcoming)

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

July 23, 1997

Jack E. Henningfield, Ph.D.
Vice President, Research and Health Policy
Pinney Associates
Associate Professor, Behavioral Biology
Johns Hopkins University School of Medicine
President Elect,
Society for Research on Nicotine and Tobacco

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

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

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

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

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

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

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

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

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

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

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

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

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

Priorities

Growing out of an ongoing review of the 20 June "Proposed Resolution"

John Slade, M.D. 7 July 1997

Here are notes related to the "Proposed Resolution" organized in a first approximation of priority.[1] Some of the elements would, in my view, actually be harmful to public health and are listed as being counterproductive.

An important element that is not reflected in the Proposed Resolution at all is how to best manage the larger context of all nicotine delivery devices, including those made by conventional pharmaceutical companies. Ken Warner, David Sweanor and I have argued that there would be advantage to a system that deals with all nicotine delivery devices on a more or less equal regulatory footing as a way to most rapidly transform the nicotine market to meet public health goals. A summary of this thinking, extended to reflect recent discussions emerging from a workshop I helped organize in Toronto last March, forms the last section of these notes.

The Proposed Resolution is not cast in legislative language and contains a number of ambiguities. It is unclear, for instance, what authority FDA would have over advertising. At one point, the document uses the term "etc." What does this mean in a legal agreement? At another, the agreement holds sacred "the sale to adults of traditional tobacco products" even as it describes giving FDA authority to mandate changes in tobacco products. Why is this not a contradiction? One must assume that these ambiguities are deliberate since the document was developed with compositional help from well staffed law firms which are intimately familiar with the ins and outs of the tobacco issues.

In important ways, the Proposed Resolution is more backward looking than forward looking from a public health perspective. It deals ~~forcefully~~ with yesterday's problems while positioning the tobacco industry favorably for tomorrow's battles.

PRIMARY

The only acceptable goal is to reduce illness and death caused by tobacco products to the greatest extent possible. The public health purpose of any legislation should be framed in the broadest possible manner: The goal is not merely to make tobacco products less toxic for those who

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[1] These notes are a companion to my preliminary notes dated 24 June.

will not stop or to have fewer kids get started. The goal is to stop the killing.

To stop the killing, the lying should also stop. Tobacco products are addictive poisons. Lies, deceptions and half-truths about tobacco, whether in word, image, brand name, official pronouncement, or otherwise, should stop. If the lying and deception continue, not only will the public continue to be confused, the regulatory job will be that much more difficult because of the doubletalk and cross purposes.

The federal government should have the responsibility to regulate all aspects of tobacco products from seed to smoke. This means that there should be a seamless ability on the part of the government to set performance standards and otherwise regulate the product and its raw materials from the farm to the retail shelf.[2] (This might require a shared authority between USDA and FDA and would likely include state authorities in some instances.) The government's ability to set these standards should be no more burdensome on the government than it is for setting standards on codeine, aspirin, eye wash or hand lotion.

Legal protection from suits in which plaintiffs have similar resources and staying power (class actions, AG actions) should only be provided if the administrative structure for long term control is solid and will really benefit public health. While there needs to be enough money flowing to the FDA and other regulators to make sure this happens, the protection of public health is is otherwise more important than the money. That is, the public health is the foremost concern. Concessions should be made on limiting legal avenues if and only if the public health is otherwise actually, without a doubt, protected by the resulting legislation.

Similarly, non-defendant companies such as Japan Tobacco and Pinkerton would be subject to powerful anti-competitive hammers under the Proposed Resolution. This extraordinary pressure (escrow account and distribution problems) can only be justified if the public health is genuinely protected by this agreement. If the public health protections are weak, or worse, then there is no justification for imposing what otherwise might justifiably be regarded as illegal tariffs

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[2] An example of the possible need for a product quality rule at the retail level is the Swedish requirement that moist snuff be kept under refrigeration throughout the distribution chain to keep nitrosamine levels low.

on international trade.[3]

THE ROLE OF CONGRESS

- Congress has long been the primary regulator of the tobacco industry. This has mainly served the interests of the industry itself. The Congress should step aside and let the FDA assume this role.

FDA AUTHORITY

This authority should be broad. Well developed processes available to all manufacturers presently regulated by FDA already provide protections to tobacco product makers against potential agency abuses. The tobacco industry has a heavy burden to show that it deserves special protections, special procedures and unusually demanding evidence standards unavailable to the makers of codeine, aspirin, eye wash or hand lotion when its cigarette brands are known to kill half of its best customers.[4]

The goal of FDA regulation in this area should be broadly defined as protecting the public health. There should be no language which limits FDA's interest to any single group such as current smokers. A rule for a fire safe cigarette may actually benefit more non-smokers than smokers. A rule to make smokeless tobacco products taste less like candy would be directed at reducing new use. It is not possible

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[3] Japan Tobacco, one of the world's largest cigarette companies, has established a beachhead in the United States. It sells the premium brand Mild Seven and the discount brand Wave. Active in the US market for several years now, JTI has established widespread distribution. JTI is a wealthy, aggressive competitor. It would be in a position to challenge any limits placed on non-defendant companies if there were insufficient benefit to public health in the legislation.

[4] The issue is who is to be trusted? If tobacco companies receive any more favorable treatment under this system than the makers of codeine, aspirin, eye wash or hand lotion, the message is that tobacco companies are to be trusted more than these other companies. The record shows that this is not good judgement.

The Proposed Resolution sets the penalties potentially faced by the tobacco industry for violations higher than those faced by other industries. Dramatic penalties are windowdressing unless there is a realistic chance to impose them for things that really matter.

to forsee all the target groups that may benefit from the regulation of specific aspects of these products, so a broad authority to protect the public health is the only appropriate guidance the legislation should offer the agency.

- FDA should have jurisdiction over all tobacco products, not merely cigarettes and smokeless tobacco products. If this is not done directly in the legislation, there should be a clearly defined pathway for FDA to assert jurisdiction over other products (cigars, pipe tobacco) when it feels it is appropriate and then to have these products come under the same set of rules as cigarettes and smokeless tobacco.

- There should be unambiguous provisions for FDA to have unlimited and continuing opportunity to learn about all aspects of tobacco product design, engineering and manufacture, from seed to smoke. This should include information about why things are done the way they are done as well as what has been thought about or tried in the past and discarded or not implemented. This includes considerations of all ingredients and processes, not merely those that happen to be regarded by manufacturers as having to do with nicotine and with the poisonousness of tobacco products.

- FDA should be able to regulate all claims made about tobacco products, not merely those which may be made for products that manufacturers self-designate as risk reduction products.[5] This includes claims embedded in brand names such as "Marlboro Lights" and "Virginia Slims".

- FDA should be able to require appropriate premarketing testing and postmarketing testing and surveillance of novel products which have the potential to reduce risks of tobacco use.

- FDA should be able to set performance standards for this industry in a manner which is analogous to the way it sets standards for other industries. Any criterion or procedure which imposes additional requirements on the agency beyond its normal practice cannot be justified for such a toxic product. Makers of cigarettes should not get procedural benefits that

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[5] The term "risk reduction product" promises more than it can deliver. "Reduced poison" better captures the actual concept here since the actual risks of interest can only be assessed after products in this category are on the market.

makers of codeine, aspirin, eye wash or hand lotion do not have.[6]

- Performance standards should include issues concerning not only the direct toxicity or addictiveness of products for continuing consumers of these products but also issues relating to the flavor, ease of use, appeal and consumer acceptability of these products. This latter authority should not be restricted to limiting the appeal of these products to those who are underage. Performance standards should include the authority to exclude certain ingredients, to set ceilings for other ingredients, and to set ceilings for chemical levels in finished products and yields in smoke tested under conditions defined by the agency. This authority should not be restricted to non-tobacco ingredients and it should be possible for FDA or a sister agency or a state to regulate raw materials such as tobacco itself and finished products until they leave the retail shelf.

- Provisions in the Proposed Resolution about cross-licensing and providing for governmental introduction of improvements not marketed by private industry are useful features.

- FDA should be encouraged to move towards a system which would permit it to apply similar standards for the protection of public health to all nicotine delivery devices, whether they arise from tobacco companies or from pharmaceutical companies. See the last section of this paper for a brief discussion of this.

- There needs to be a definition of what an existing product is and what a new product is. FDA should be able to examine changes in process or ingredients to judge whether these may have an adverse effect on public health. This judgement should include considerations of whether a proposed change might increase the appeal of the product to certain groups such as kids. The agency should be able to take appropriate action if it finds proposed changes will have an adverse effect on public health.

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[6] There is no public health justification for requiring the agency to undertake a separate consideration of the effects its rules might have on contraband or on the use of unregulated tobacco products. The agency has already shown a sensitivity to these factors in its discussion of the existing rule. There is no reason to believe that FDA will not continue to take these issues into consideration as it regulates these products.

- There should be a process whereby growing and curing of tobacco can be regulated, perhaps through USDA in cooperation with FDA. This process should not depend on the price support program since this program may not continue to exist. Provisions under this process should apply to imports of tobacco as well as to domestic production.

- It is unclear whether the proposed agreement permits FDA to regulate advertising for tobacco products. FDA should have full, clear and broad authority to regulate advertising of tobacco products. The Federal Trade Commission has consistently shown over a period of sixty years that it cannot do an effective job of this.

- FDA should have the clear authority to regulate the content, size, placement, and design of warnings and other consumer information on tobacco product packages and package inserts. The Proposed Resolution only gives it authority to change the wording of a Congressionally mandated design. This is an example of the sort of Congressional regulation of this industry that has been so damaging to public health over the years.

- FDA should have the clear authority to regulate the flow of information about tobacco products from manufacturers to the public. This authority should include the ability to require disclosures about any ingredient, including any ingredient derived in any way from any species of Nicotiana when, in the view of the agency, such disclosure will advance a public health purpose. This authority should also include the ability to require disclosures about specific chemical content and yields, including tar, nicotine, carbon monoxide, as well as any other material or set of materials when the agency believes that such disclosure will advance a public health purpose. The ways in which information should be disclosed can vary from being available on request from manufacturers or from the government all the way to being required on packages, package inserts and advertisements. Part of this authority should be the ability to develop and standardize tests for specific chemicals and sets of chemicals (i.e. FDA can develop a successor to the FTC test).

- FDA should have clear authority to regulate the availability of tobacco products. The national licensing system seems a good starting point. There should be flexibility in the system so that there might be the ability later on to limit sales to certain kinds

or numbers of outlets.[7]

- FDA should have adequate funding for these activities.

OSHA

- Environmental tobacco smoke should be removed from the workplace. Exceptions should be few and should not include restaurants, bars and casinos. Consideration should be given to providing workers in exempt businesses with protections which, for example, could provide for work-related disability payments should a worker develop an ETS-associated illness.

FUNDING

- In addition to funding of FDA's activities, there should be funding for public education about tobacco (not limited to a kids campaign) and there should be monies provided to states for tobacco control activities. States should have broad discretion in how to use these monies.

- The amount of money to be paid under the Proposed Resolution is relatively low. If public health measures are successful, the payments will lessen over time. The payments are structured more like a tax than a fine. I would prefer that the payments be substantially larger and that they be structured more like a fine.

UNWANTED PROFITS

- The "look-back" provisions, which ostensibly make tobacco manufacturers responsible for their contributions to underage tobacco use are so weak in the Proposed Resolution as to be of no practical value to public health. As written, they probably are counterproductive since they have the potential offer important potential public relations opportunities to tobacco companies. This approach would have utility, however, if it had the following characteristics:

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[7] In Ontario, some communities have suppressed sales to minors to the 5% level but have still not seen any reduction in tobacco use rates among the young. It may be that there are simply too many retail outlets for even a 95% effective program to be of benefit.

- It should be called something more descriptive than "look back". "Unwanted profits penalties" better captures the flavor of what this is about.

- Tobacco companies should forefit all profit on all tobacco sales to minors right away and for the future, perhaps even going back a reasonable number of years for the first payment, adding interest to the back payments.[5]

- Measure tobacco use in the past 30 days, not merely daily use.

- Measure brands used by kids so that actual market share of the youth market can be assessed and apportioned to each manufacturer. The "brand most recently used", or the one in the kid's pocket at the time the survey is done, or the last brand purchased, would likely be a better measure to arrive at market share than "usual brand".

- Require each company to report to its shareholders its proportion of the underage market in tobacco products over time and in comparison with the rest of the industry with an explanation of the steps the company is taking to improve its performance.

- Measure progress in terms of reduced numbers of kids using tobacco products, not in terms of reduced rates of kids using.

- In addition to the unwanted profits levy, provide for penalties if targeted reductions in underage tobacco use are not met which are a realistic deterrent and which are not easily avoided.

- If there are forgiveness provisions, give non-profit organizations involved in tobacco control standing and incentives (such as attorney fees and an award if successful) to challenge the forgiveness.

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[5] Several years ago, I was on a TV interview program with Walker Merryman of the Tobacco Institute. I asked him if his clients wanted to sell cigarettes to kids. He said, "Of course not." I then asked if they wanted the money they made selling cigarettes to kids. He said, "No." I suggested that his clients should then give these unwanted profits to public health agencies for prevention. He said, "That's complicated." The present legislative opportunity can cut through Mr. Merryman's reservations.

- Experienced epidemiologists such as John Pierce (UCSD) and Gary Giovino (OSH) can provide information on the study design necessary to capture the data needed to administer this provision effectively.

- One of the potential strengths of this approach is that it may be a fairly direct way to force changes not only in advertising but also in product design. For instance, how successful could UST be in claiming it had done all it could to stop kids from using its products if it still had Skoal Cherry Long Cut on the market? This same approach could also possibly be used to force changes in minimum package size or in other elements of pack design. The criterion should not be "does this primarily appeal to kids?" but rather it should be "does this practice or feature draw kids in or in any way make it more likely that kids will use this product?"

TREATMENT

- There should be substantial funding for treating nicotine dependence. This funding should be actively administered by DHHS or another suitable entity to assure that it will have the greatest possible public health benefit. There are issues of quality assurance, availability, accessability, and range of services suitable to the range of severity of nicotine dependence. Most treatment research in this area has been done on primary, or at best, secondary treatments. These methods are frequently not suitable for the most heavily addicted and for those who have complicating conditions such as depression or another mental illness.

RESEARCH AND EVALUATION

- There should be substantial funding of research and evaluation efforts aimed at achieving the public health goal of reducing illness and death from tobacco products. The Proposed Resolution has a provision for a "Public Health Trust Fund". This must have a primary mission of reducing illness and death from tobacco products and must not be limited to "medical research". This research need will be ongoing as long as there is a tobacco problem. Oddly, the "Public Health Trust Fund" seems to be time limited. It should not be.

The achievement of clear FDA authority in this area, the provision of support for treatment, and other features will increase the need for well-designed, focused policy research in numerous areas of regulatory, general public health and clinical concern. Over the past seven or eight years, the policy field has benefitted enormously from research funded by private foundations, state governments and the federal government. The next stage of work in this area will require a substantial increase in policy research funding if we are to be able to take the best advantage of the opportunities that this legislation potentially provides.

Similarly, with the prospect of an iterative process to regulate this industry and the availability of resources for treatment and other prevention efforts, there needs to be a careful evaluation process to make sure that the steps taken are the ones which best protect the public health.

These needs imply major expansion of the activites of the Office on Smoking and Health, the NCI, state and private research and grant-making organizations to achieve these ends. Diverse funding sources will best assure the necessarily diverse research. Some undertakings, such as frequent population surveys, may best be done by OSH, but the need for its research instruments to pass OMB scrutiny may prevent these from achieving their full potential.

INTERNATIONAL ISSUES

- Nothing we do should make it more difficult for other countries to control their tobacco problems or for citizens of other countries to use the judicial system here or abroad for relief. There should be provisions for extensive and ongoing international public health exchanges about controlling tobacco the tobacco epidemic.

- I have heard arguments both ways about whether performance standards for tobacco products should apply to products which are made here for export. FDA has authority to regulate pharmaceutical products made here for export. Why should cigarttes be any different? I have not found arguments that exports should be excluded persuasive. The double standard is too large.

CONTRABAND

- The Proposed Resolution provides several important incentives for the creation of a black market. Besides the obvious incentive of simply undermining performance standards, payments under the Proposed Resolution are directly proportionate to domestic production. Reimportation of exports for domestic consumption would lower payments the companies owe.

- There should be a review of relevant laws about smuggling and a substantial strengthening where appropriate.

SECONDARY

LEGAL PROTECTIONS

- Legal protections to assure that lawsuits can still be brought against tobacco companies for product liability are important but not as central to this as assuring the protection of the public health. If public health structures are not adequate to reduce illness and death, however, the public health need for lawsuits will increase. So this aspect is secondary if and only if the primary objectives are achieved.

STRONG ARMING NON-DEFENDANT MANUFACTURERS

- Non-defendant manufacturers and importers should only be subjected to the onerous terms proposed if the deal actually has a primary public health purpose and the strength to accomplish that.

ADVERTISING LIMITS IN THE PROPOSED RESOLUTION

- The specific measures in the proposed agreement to reduce the appeal of tobacco product advertising to kids are appealing, but there are at least two other ways to achieve the end. One is through the direct regulation of tobacco product advertising by the FDA. Putting these measures in as settlement terms avoids legal challenges that an FDA rule would face, however.

  Another way to avoid legal challenges would be to give the "look back" provisions enough strength that companies would have genuine incentives to clean up the way they do business. By simply making them pay money the more their products are used by kids, they could

have the incentive to do these things voluntarily without our having to accept it as part of a settlement. This possibility means that the public health side does not have to compromise on the FDA authority just to get the industry's cooperation on voluntary advertising limits through settlement to avoid court challenges.

We should be realistic about what actual improvements in public health are likely from the advertising limits listed in the Proposed Resolution. In Canada, there was a more complete ad ban for 8 years (enacted with none of the concessions found in the Proposed Resolution). The ban was evaded in various ways. I do not believe that Canadian public health officials attribute much of the decline in tobacco use there to the ad ban. Price increases were far more important. Ad limits are helpful, but they are far from the whole picture. There is, at the same time, little credibility in a tobacco company trying to justify advertising that reaches and appeals to kids.

SETTLEMENT PAYMENTS

- Payments should not be a simple function of units sold. It is inappropriate to insulate sister operations from obligations to make these payments since the sister operations often came into existence because of retained profits from the domestic tobacco operation.

TERTIARY

INDUSTRY DISCLOSURES

- The disclosures may be useful; they certainly will be interesting. As proposed, though, they seem more limited than they should be. Of greater importance for public health, however, will be the free and open sharing of complete information about products with the FDA.

SALES TO MINORS

- Restrictions on sales to minors are useful but under the Proposed Resolution have the unfortunate potential to become the major focus of tobacco control efforts. This draws attention away from those measures which have greater potential to reduce illness and death. Increased awareness about tobacco sales to minors has helped highlight numerous facets of the tobacco

problem, but this issue should not be the centerpiece of public health efforts.

It is easy to imagine the tail wagging the dog here. One possibility is that local laws against posession and purchase by minors will proliferate, further diluting efforts to stop the epidemic.

COUNTERPRODUCTIVE

There are certain elements of the Proposed Resolution that, in my view, would leave the public health worse off than it is at present. These include:

VOLUNTARY CORPORATE RESPONSIBILITY MEASURES

- The industry has used voluntary measures for decades to accomplish its public relations objectives without having to stop killing its best customers. This is the latest incarnation.

- Without genuine confession, which the industry's lawyers won't let happen unless there is absolute immunity from suit, these measures will be windowdressing. They will be especially pernicious windowdressing because they will further cover up the deceit. The language will be about preventing kids from starting, but the talk will never focus on the fact that the only real reason this is sound policy in the first place is that it will lead to fewer deaths.

- It is the appearance of reform minus the substance.

DISSOLUTION OF THE TOBACCO INSTITUTE AND THE COUNCIL FOR TOBACCO RESEARCH

- This seems to me to be smoke and mirrors. No one at TI is going to lose a job.

TAR CEILING OF 12 MG USING THE FTC TEST METHOD

- We should bury the FTC test, not enshrine it in a tar ceiling. If FDA has the proper authority, and if it is actually a good idea, it can do this on its own, without it being legislated by Congress.

BOTTLENECKS AND BURDENS

- The ingredient approval process outlined in the Proposed Resolution includes a potential major bottleneck: FDA might well face hundreds of submissions at the end of the five year grace period with only 90 days to review all of them. This should be avoided. The agreement should be reviewed to see if other such bottlenecks are present.

SOME INDUSTRY ARGUMENTS

Contraband

Black markets are not magic. They can be manipulated up or down by those with an interest in doing so. They will be part of the issues to be faced in the setting of effective regulation; they cannot be avoided. They must be managed so they do the least harm.

The tobacco industry has exploited black markets to erode trade barriers (South America and Asia) and to undermine government tax policy (Canada). It has succeeded at these ploys without having had legislation in hand which required government to avoid black markets at all costs in formulating policy. The way the Proposed Resolution treats contraband and other tobacco products makes it highly unlikely that performance standards not advantageous to the industry could ever be implemented.

Prohibition

Bloody shirt. The industry says it doesn't trust the FDA, and it uses the specter of prohibition as its rallying cry. However, performance standards are about much more than the regulation of nicotine levels.[9]

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[9] It is unfortunate that the media shorthand for performance standards has become control of nicotine content. What the discussion should be about is how can manufacturers assure that their products are the least harmful possible. While tobacco products will never be wholesome, they can be less poisonous and less likely to attract novices. In a future market, there may well be alternative devices available whose use would be far less hazardous than current products and whose availability might permit the FDA to require that the nicotine content of existing products be lowered. However, this is speculative. Immediately at hand are a number of opportunities to require product modifications that, while modest, are in the

Fundamentally, though, the industry shold only reap what it has sown here. The industry has shown that it cannot be trusted. The legislation needs to tilt towards trusting either the industry or trusting the FDA. The FDA, at least, operates in the open, and this should improve the confidence the industry should have in its being able to trust the agency's taking a conscientious and appropriately balanced approach to these problems.

Job loss

Any changes in employment from a smaller industry will be gradual. The money that presently buys tobacco products will be used for other goods and services so the economy as a whole will not be harmed. These are not unusual conditions in a dynamic economy.

To the extent that there are important dislocations, these can be dealt with by subsidies to those affected. There is a long tradition of these sorts of accomodations being made in other situations, such as the closing of military bases.

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right direction. Others will likely come from the FDA learning more about how tobacco products are made and how they might be made.

Managing the Future Market for Nicotine Delivery Devices

As long as tobacco products are available, there will be some who cannot stop using nicotine. Both conventional pharmaceutical companies and tobacco companies (which are, after all, merely unconventional pharmaceutical companies) are developing and have available a range of nicotine delivery devices that hold promise for public health. Both the present system for regulating these devices and the system contained in Proposed Resolution are upside down: the most toxic products have the least oversight.

Prevention and cessation will always remain the bedrock strategies for controlling the tobacco epidemic, but it is clear that there also needs to be a range of alternatives for those who are otherwise unable to stop using conventional products. While the Proposed Resolution acknowledges this by proposing processes for FDA to regulate less poisonous devices from tobacco companies, the Proposed Resolution overlooks the potentially important role conventional pharmaceutical companies might play in this.

Conventional pharmaceutical companies presently have FDA approval for a range of devices that delivery pure nicotine (patch, gum, nasal spray and inhaler). All of these approvals are based on a cessation indication and each of these products is expensive and hard to get compared with cigarettes and smokeless tobacco.

Several companies are exploring "exposure reduction" as a new indication for these and related products. This approach, which envisions use of nicotine replacement along with tobacco products as a bridge to the gradual achievement of abstinence and the more prolonged use of nicotine replacement compared to current labeling, raises important policy issues which should be examined in light of the Proposed Resolution.

It is likely that, in coming years, the continued use for an indefinite period of time of a pure or nearly pure nicotine delivery device will become an acceptable alternative to the use of conventional tobacco products. The FDA should have the tools and the flexibility to foster an optimal mix of products from both conventional pharmaceutical companies and tobacco companies to meet this market if this is the direction that clinical practice takes.

Under the Proposed Resolution, however, there would be a markedly different set of standards for a conventional

pharmaceutical manufacturer compared to a tobacco manufacturer. The former would face a lengthy approval process in order to offer, say, a mint flavoring for nicotine gum, while the latter could put whatever flavoring it chose into its products with no need to show the FDA that its flavoring would not appeal to childen.

A goal of tobacco product regulation should be that all makers of nicotine delivery devices eventually be subject to similar standards. They compete, after all, for the same market. The standards may never be identical, but they can, over time, converge. Any legislation in this area should insure that FDA has the flexibility to make this happen.

The regulatory structure for nicotine delivery devices is upside down. The most poisonous and addictive products are the least expensive, the most widely available and the most attractively packaged. Through coordinated federal policies, including taxation and product regulation, the least toxic products should eventually become the most available, the least expensive and the most attractively packaged.

A key element towards insuring that this future is possible is a structure for product regulation that applies similar rules to products from conventional pharmaceutical companies and to products from the unconventional companies. Moreover, the general direction of such a convergence should be upwards, towards the standards presently applied to products from conventional pharmaceutical companies.

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July 2, 1997

Jerold Mande
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Regarding: Evolution of the Proposed Tobacco Settlement; Establishing a Sound Agenda

Dear Jerry:

As I mentioned in my June 24th letter to you on the Proposed Tobacco Settlement, I believe that we are faced with a historic opportunity to significantly turn back the current of tobacco-related death and disease as we enter the new millennium. But the short- and long-range outcomes of this Settlement will depend on our establishing and following a sound agenda of tobacco control and our ensuring that no details of the final settlement will later undermine that agenda. My stance is neither stridently for or against the Proposed Settlement. Instead, I view it as a potentially useful vehicle for necessary change; it needs to be modified appropriately, but it also needs to be headed in the right direction.

The major advantage of developing a Tobacco Settlement that the public health community and the legislative and executive branches can all support is that it spares tobacco control the judicial alternative—namely, litigation that could continue for many years without making any significant contributions to the public health. With the President and Congress involved, public policy is being made and made clear. It seems evident that any responsible policy should guarantee—if not expand—the authority of Food & Drug Administration (FDA) over the marketing of nicotine-delivering tobacco products. This authority was claimed in August 1996 with the FDA Final Rule, but was later substantially restricted by the Greensborough Court. However the White House responds, the settlement provides an invaluable opportunity for the executive branch to analyze and formulate key strategies on tobacco control.

The agenda behind the Proposed Settlement seems significantly different from the agenda motivating earlier tobacco control efforts. Presently, the primary aim of the Proposed Settlement is to compensate States for the health costs of smoking; secondarily, it includes some measures that are expected to reduce the magnitude of public harm caused by tobacco use. This emphasis may have been an inevitable consequence of the negotiation process. After all, the Settlement resulted from Attorney General (AG) lawsuits and was negotiated

largely by parties to the AG suits. Yet the emphasis on the financial aspects of compensation has contributed to wariness that the Proposed Settlement might amount to a cynical licensing agreement, in which tobacco companies pay for the continued right to find even more creative ways to market their lethal products and well into the forseeable future. While the Attorneys General are attempting to settle once and for all the damages due to citizens of their States, they have overlooked several costs not borne by the States, as well reparations due to other, equally deserving parties.

The Centers for Disease Control and Prevention (CDC) estimated total direct medical costs attributable to tobacco use at $50 billion per year; CDC calculated that the indirect costs of tobacco (among them lost productivity) amounted to an additional $50 billion per year. Given these numbers, the Proposed Settlement covers only one-tenth to one-fifth of the total costs of tobacco to the US market. It precludes many parties who are directly and indirectly paying for the costs of smoking—insurance companies, for example, and employers—from recouping their expenses.

The funds the tobacco companies have agreed to allocate to smoking cessation treatments provide probably one-tenth to one-fifth of an appropriately applied cost of reimbursement. If 20 million smokers try to quit annually (a number slightly greater than CDC estimates for annual quit attempts made over the last decade), providing even $500 to each of them for cessation treatment would cost tobacco companies $10 billion—considerably more than the $1.5 billion now proposed to help smokers end their addiction. Certainly, additional funding is likely to expand treatment access and utilization. Following are some questions that pertain to this expanded cessation treatment:

- How can funds be used most efficiently to expand access to and utilization of cessation treatment?
- Who should administer the funds?
- What should be the standards for reimbursing cessation treatment services and medications?
- How can smokers be given incentives to quit and aided in their quit attempts?
- What will be the standards for payment for treatments of special populations when clear guidelines do not exist for their treatment? For example, how should adolescents and addicts of other drugs of abuse be treated?
- How much support should be provided to each smoker for a given treatment and for treatments over the course of that individual's life?

While the issues of costs and payments due are obviously central to any settlement, it is imperative to remember that improved health for all Americans (including current smokers) is the ultimate goal.

We must pay close attention to the agenda this Proposed Settlement might shape for generations to come. We need to focus on the public health outcome, whatever its cost. I would recommend that the Settlement be made in accord with goals of the FDA Final Tobacco Rule: Above all, the purpose of this Settlement should be *to reduce the death and disease caused by tobacco use, and to thereby enable our citizens to enjoy healthier, longer and more productive lives.* With this kind of public health mandate, the emphasis

and tone of the Proposed Settlement would be radically altered. Instead of a subpart addressing public health consequences, the entire document would focus on public health approaches and implications. Financial issues would become subsidiary. If we are to stay committed to the public health, we must attempt to predict and evaluate both the short- and long-term health implications of any settlement. Several research approaches are needed to meet that end.

Just as successful consumer product companies track consumer use and attitude so that strategies can be adjusted within months of a market trend emerging, so the Settlement too would need a methodology to track and respond to undesirable trends. This would represent a drastic evolution in our present surveillance capabilities. Reporting data on adolescents just recently became available for the prior year; reporting data on adults becomes available only once every three years. We currently have no mechanism to adjust public health messages and consumer approaches mid-course. The public health implications of strategies such as the Joe Camel campaign take as many as five years before they are realized. During this time, there is little means of response. There has to be a way to monitor the reaction to advertising and promotion by tobacco companies and pharmaceutical manufacturers alike.

In order to guarantee that new tobacco industry strategies do not produce lasting adverse effects (and that pharmaceutical companies can respond creatively to waxing and waning tobacco dependence), we need to create new surveillance systems to supplement existing ones. Among them should be a rapid reporting system that produces results at least quarterly, with reports given on smoking uptake; reports on a wider range of levels of smoking (and not only by daily smokers); reports on the number of quits attempted in a given population; and reports on market activity with all forms of nicotine consumption, including the nicotine gum and patch. This information is also vital to the design and interpretation of research into both smoking uptake and cessation.

Supportive, integrated and complementary research is essential across a variety of disciplines. The terms of the Proposed Settlement imply that our understanding of smoking prevention and cessation treatment would enable us to achieve target goals, given sufficient resources. This is simply untrue. There are considerable gaps in our understanding of tobacco dependence, especially of growing tobacco dependence in youths. Even under the most optimistic scenario, with tobacco use by youth reduced 50% in the next 5-10 years, 500,000 young people will become chronic smokers each year, with one-third to one-half of them later dying of tobacco-related disease. Furthermore, the extent to which the tobacco industry can effectively recruit adults to cigarette smoking remains unclear. It is plausible that as barriers slow cigarette marketing to a younger and more impressionable group, there will be increasingly sophisticated efforts to persuade adults to initiate smoking, or to encourage former smokers to resume that activity.

There is a good deal of research yet to be done, but clearly, some research demands are more pressing than others. High research priorities include:

- Research on the etiology of nicotine dependence in youth and adult onset of tobacco use.
- Treatment for tobacco-dependent youth interested in quitting.
- Treatment for special populations, including people with current or past psychiatric disorders and histories of substance abuse, diverse ethnic and cultural populations, users of tobacco products other than cigarettes.
- Research on the degree to which genetic constitution alters susceptibility to developing nicotine dependence and/or modulates the ability to quit.
- Determination of the functional significance of alterations of brain structure and function produced by nicotine exposure.
- Thorough characterization of the dose-related behavioral effects of nicotine and other tobacco and tobacco smoke constituents which contribute to the dependence process.

In developing a research agenda, I would encourage you to take advantage of research organizations such as the College on Problems of Drug Dependence (CPDD) and the Society for Research on Nicotine and Tobacco (SRNT). Although it is quite young, SRNT is also the foremost international forum for nicotine and tobacco research; it involves a number of professionals committed to focusing and disseminating the latest scientific findings on the understanding, prevention and treatment of tobacco dependence. Its past presidents include Drs. Ovide Pomerleau, John Hughes, and Neal Benowitz. Its current president is Dr. Maxine Stitzer; I am its president-elect. All of these scientists have been at the forefront of tobacco dependence research. In addition, Dr. Kenneth Keller of Georgetown University is now taking the lead role at SRNT in the development of an agenda for research that could support the goals of the Tobacco Settlement.

I have included a list of the names and telephone numbers of some of the pre-eminent authorities in this field, in case you should want to contact them. I hope this information is useful. Please let me know if I can be of further assistance to you.

Sincerely yours,

Jack

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Meeting Report:
London Anti-Smoking Summit

Date: 14 July, 1997
Place: London
Title: Anti-Smoking Summit (Subtitle: "Dying for a fag")
Convenor: Department of Health, Tessa Jowell, MP, Minister For Public Health

Purpose: The purpose of the meeting was as follows:

1. To signal the government's strong intent to develop a course that will help dramatically reduce cigarette smoking among youths and adults alike though prevention, cessation and possibly harm reduction approaches.
2. Obtain advice and support from many of the world's leading tobacco experts and policy makers.

Initiate the development of a White Paper which will serve as the foundation for developing a legislative and regulatory course which will then be presented by the Queen for consideration by the Parliament. The paper is contracted for completion by fall this year.

Note: This issue is part of the "platform" of the new Prime Minister, Tony Blair, and is considered as an important departure with the previous Conservative Government, which was viewed to be committed more to the tobacco industry than to the tobacco-caused disease reduction. This sense of shift seems to be felt in all levels of government and civil service staff. At the opening of Parliament on May 14, 1997, the Queen announced that a new legislation to curb tobacco and reduce disease would be drafted. This meeting is a continuation of that process.

Senior British Government Officials: Tessa Jowell, MP, Minister for Public Health; Frank Dobson, MP, Secretary Of State For Health; Padraig Flynn, Commissioner Responsible For Employment and Social Affairs; Sir Kenneth Calman, Chief Medical Officer ("Surgeon General") and at least 8 additional ministers of various departments, as well as lead officials representing various government departments, e.g., the Director General of the Advertising Standards Authority, Ministry of Agriculture and H.M. Treasury.

Participants: Leading researchers from the United Kingdom included Ann McNeill, Martin Jarvis, Michael Russell and Sir Richard Doll. Researchers and policy makers from other countries included Thomas Glynn (National Cancer Institute), Gregory Connolly, John Slade, David Sweanor, Karl Fagerstrom, David Simpson and Garfield Mahood. Major health organizations from the United Kingdom and around the world included the Association for Smoking and Health (ASH), British Medical Association, National Health Services, and the World Health Organization (WHO).

Format: A morning plenary session was held at the Museum of the Moving Image with official statements and directives, and a press conference which incorporated invited statements and endorsements from health and policy leaders around the world. A strong directive from the Prime Minister, Tony Blair, was provided. The French Minister of Health had sent in a strong

letter of support, but could not attend as it was Bastille Day in France. The afternoon session was convened at Regents College and consisted of a brief plenary session with directives by Sir Kenneth Calman to provide the initial material for a White Paper. We were then dispersed into two-and-a-half hour work-groups ("syndicates") divided into 6 topic areas. Each syndicate's main conclusions were presented and discussed in the final plenary session.

Plenary Session Highlights:

Frank Dobson, MP, Secretary of State for Health, provided a strong statement of commitment by the Prime Minister and the government to enact legislation leading to stronger tobacco control, prevention, cessation and tobacco-caused disease reduction. His understanding of the power of nicotine, the high toxicity of tobacco smoke and the economic, regulatory, social and legal complexities of tobacco and health issues was admirable and clear.

Tessa Jowell, MP, Minister for Public Health, reviewed the various statistics and trends and noted that 70% of smokers in the United Kingdom were interested in quitting. In this context, she highlighted the importance of integrated approaches including education, increased taxation, marketing restrictions on tobacco products (e.g., banning tobacco sponsorship of sports and arts) and providing cessation treatment. She stated that the tobacco issue was her number one priority.

Padraig Flynn, Commissioner Responsible for Employment and Social Affairs, described the adverse socially stratified effects of tobacco use and disease which particularly affects the already economically disadvantaged persons. He also emphasized the importance of protecting the young from addiction by reducing incentives to smoke ("appeal") and protecting people from passive smoke exposure.

Alexander Macara, Chairman of Council, British Medical Association, discussed the addictiveness and toxicity of tobacco and the importance of treatment and prevention in disease reduction. He emphasized the importance of increasing the availability of nicotine replacement therapy (NRT) and decreasing the cost of NRT relative to tobacco as might be achieved through increased tobacco taxes.

Claire Rayner, Writer/Broadcaster and a tobacco control advocate, talked about the need to provide positive incentives to encourage smokers to try to quit smoking and also offer assistance to help them remain successful in quitting.

Richard Branson, Founder and Chairman of the Virgin Group of Companies, offered an extraordinarily insightful analysis of the tobacco companies' marketing efforts, the social responsibility of such efforts for an addictive and toxic substance and the need for recruiting private industry to take up sponsorships of sports and arts which currently depend on tobacco funds. He suggested Virgin Air, Records, etc., as a sponsor of organizations through a tobacco "rival fund". He also challenged the government to put back its 125 million "ill-gotten" tax revenue pounds into health promotion efforts like done in the states of California and Massachusetts.

The open discussion moderated by leading News Presenter ("Anchor"), Jon Snow, brought out an interesting range of opinions in support of the complexities of the issues related to tobacco from experts, leaders, Ministers and regulators from areas as diverse as sports, snooker gaming, the cultural arts, outdoor advertisers (who requested phased implementation of ad bans but did not oppose them), Formula 1 team racing representatives and World Health authorities.

Afternoon Session: White Paper development at Regents' College

Six working groups (syndicates) were each charged with laying the foundation for a White Paper which according to Sir Calman, should include the strategies, tactics an logistical needs to achieve reduction of tobacco use and associated disease. A briefing paper had been drafted and provided to each working group to assist them in making progress on issues and questions of particular concern to government in its formulation of policy. Some of the main agenda items and conclusions of the working groups were as follows:

- The scope of the advertising ban

  Major Questions: Addressing issues such as how we should define tobacco advertising for these purposes. Where should we draw the line and what can we learn from the experience of other countries? How can we protect sporting or arts events from damage resulting from a loss of tobacco sponsorship?

  The group recommended an exceedingly broad ban on advertising, marketing and various tobacco product branding approaches including sports sponsorships.

- Consumer protection issues

  Major Questions: Do variations in the age of legal purchase in different countries produce different outcomes for young people smoking? Are restrictions on vending machines or licensing agreements for retailers of any value? What warnings on packets and the information about the contents of cigarettes are provided in other countries.

  This group recommended an overhaul of tobacco product labeling and regulation, increased minimum age of tobacco purchase, and new tactics to reduce purchase of tobacco products by underage persons.

- Price, tax and fiscal measures

  Major Questions: What can we learn from other countries about their policies? How have they dealt with the need to increase tobacco prices without increasing problems such as smuggling?

  This group recommended increased tobacco taxes with new funds to provide transitional replacement of tobacco company sports and arts sponsorships, education and treatment support for lower-income smokers. The importance of the European Community and Global issues were emphasized as was the importance of thoroughly and scientifically evaluating alternative nicotine delivery systems from tobacco companies (this recognized

that such evaluation is already in place for pharmaceutical company's developed products).

- Public Education

  Major Questions: What is the effectiveness of different types of mass media programmes? Can we develop community level interventions for the groups most at risk?

  This group recommended the importance of new and broadly disseminated educational approaches with surveillance-based monitoring to evaluate progress and modify to maximize their benefit.

- Smoking in public places

  Major Questions: What has been tried elsewhere in the world either by voluntary agreement or by statutory means? How effective have different strategies been and what is realistic in terms of public opinion and practicability?

  The importance of increased measures to prevent public smoking complemented by systematic approaches to "demoralize" public smoking (e.g., via media) was emphasized.

- Helping people stop smoking

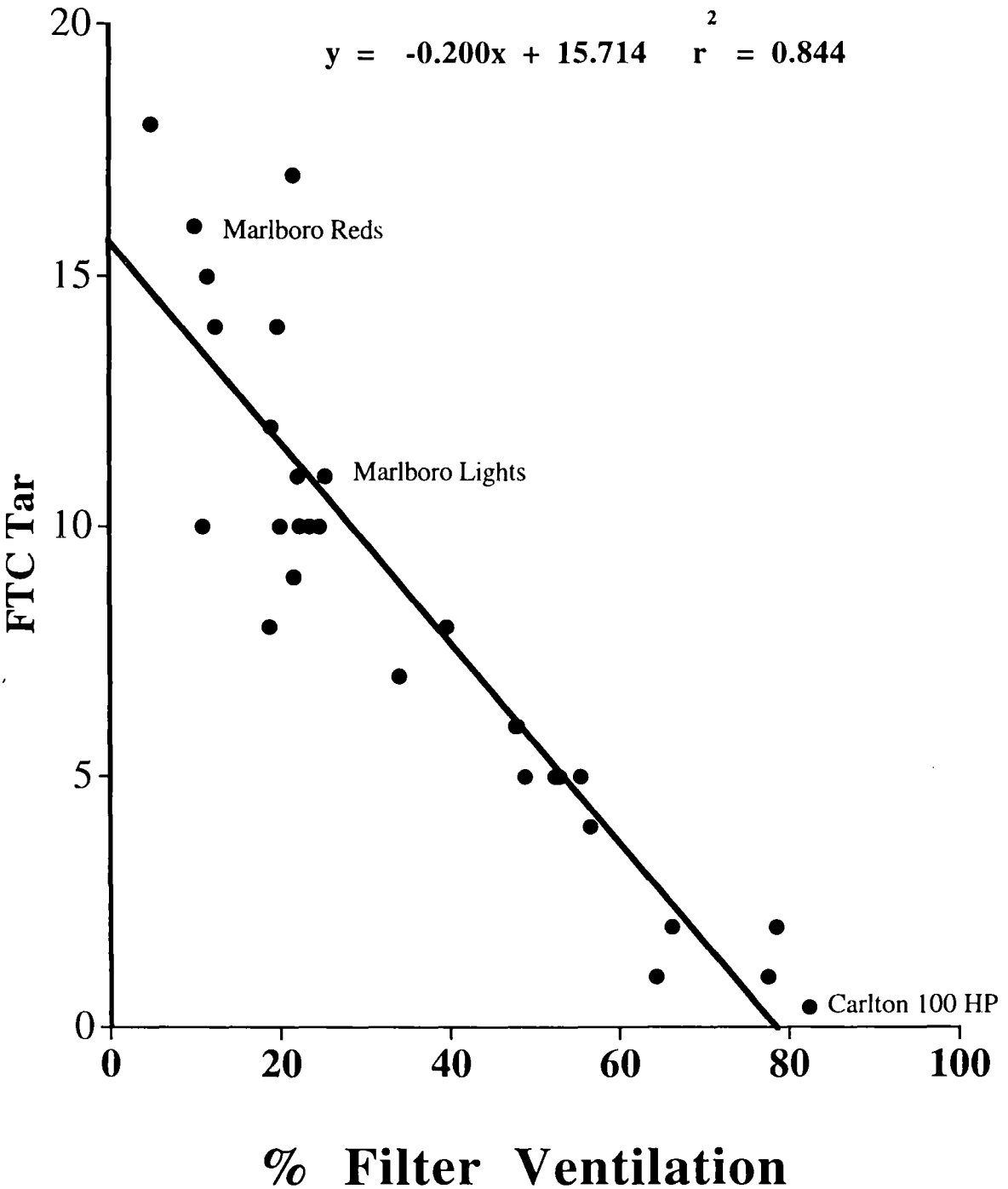
  Major Questions: What can health professionals do? Are particular techniques more helpful than others? What role can nicotine replacement therapy play? Can we take sensible steps to reduce harm by looking at the contents of cigarettes, particularly tar and nicotine?

  This group broke its mission into cessation and harm reduction approaches-
  Cessation: Development of smoking cessation infrastructure to put hot lines, clinics, and nicotine replacement medications within ready reach of those who could benefit.
  Harm Reduction: This group emphasized the importance of providing accurate data on existing and new tobacco company products with an emphasis on predicted comparative consumer exposure to toxins with consistency ("level playing field") provided across all forms of nicotine delivery (e.g., cigarette and gum), by regulating all forms of nicotine under a single agency (e.g., UK/EC equivalent to FDA).

Conclusions: This Summit was extremely well organized, conducted and attended and should provide a strong base of science, health and political support, for new government regulations that should contribute to reduced appeal and youth access to tobacco products, improved access to cessation treatment and incentives for private-sector based harm/exposure reduction approaches. As a footnote to this latter point, the intent of the Health Authority Department Staff is to quickly finish and publish a paper based on the November, 1996 seminar on alternate nicotine delivery systems and harm reduction approaches. The strategy appears well conceived to produce lasting regulatory changes as opposed to a new "Smoke and Mirrors" anti-smoking campaign. Individuals at all levels of the process are paying attention to global developments, e.g., FDA Regulation and the "Tobacco Settlement" negotiations in the United States and the new product labeling and marketing restrictions in Canada and Australia. In turn, this process is

likely to have reciprocal impact on other nations, both progressive (e.g., United States and developing nations), as well as international organizations such as WHO. The process is forward looking, and anticipates continued change and evolution of nicotine delivery products, treatment approaches and tobacco marketing strategies and tactics. Participants were invited to continue giving their input to the process. Copies of the agenda, participant list, background paper and prepared statements are available.

Tar yields as a function of filter ventilation



Lynn Kozlowski & Nick Mehta
Penn State University, July, 1997

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

CHALLENGES TO NIDA NICOTINE RESEARCHERS

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

COGNITIVE EFFECTS OF ADMINISTRATION/WITHDRAWAL

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

PREVALENCE: SOCIETAL DETERMINANTS

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

- A model for other drug abuse

YOUTH

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

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

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

CO-MORBIDITIES (SUBSTANCE AND AFFECTIVE)

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

DIAGNOSIS AND TREATMENT

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

MEDICATIONS DEVELOPMENT

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

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

July 23, 1997

Jack E. Henningfield, Ph.D.
Vice President, Research and Health Policy
Pinney Associates
Associate Professor, Behavioral Biology
Johns Hopkins University School of Medicine
President Elect,
Society for Research on Nicotine and Tobacco

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

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

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

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

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

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

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

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

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

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

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

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

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

A Proposal to Develop Meaningful Labeling for Cigarettes

SINCE the 1980s, tobacco researchers have understood that the advertised nicotine-yield ratings of cigarettes do not accurately predict nicotine intake by individual cigarette smokers.[1-5] Cigarette smokers obtain an average of 1 mg of nicotine from each cigarette they smoke, whether the nicotine yield is 0.1 mg or 2 mg.[4,6] However, smokers with whom we have spoken believe that their "light" or "ultralight" cigarettes are providing them with substantially lower doses of nicotine and other constituents of tobacco smoke. These smokers seem to assume that nicotine-yield ratings are equivalent to the content ratings provided on food products, and they are often distressed to learn that nicotine-yield ratings are not indicative of how much nicotine they can obtain.

We propose a new strategy for testing and labeling cigarettes that would provide consumers with improved information about how much nicotine they will absorb by smoking a particular brand of cigarette. Our proposal is roughly parallel to the approach of the Food and Drug Administration (FDA) for labeling food products with respect to constituents such as sodium and fat.[7]

Problems With the Present Rating System

A variety of terms are commonly misused in discussions of nicotine ratings. Most fundamentally, cigarette nicotine *content* is confused with cigarette nicotine *yield*. The nicotine content is the total amount of nicotine present in the tobacco cigarette. Nicotine yields are derived from tests using smoking machines that were originally developed to provide standardized comparisons of the characteristics of tobacco smoke from different strains of tobacco.[8] Unfortunately, neither content nor yield ratings accurately predict how much nicotine the individual is likely to absorb from a cigarette.[2-4]

The present testing method entails inserting cigarettes into the ports of automated systems, which then draw in smoke according to a set of parameters generally referred to as the Federal Trade Commission method.[9,10] According to this method of determining yields, one 35-mL puff of 2 seconds' duration is taken every minute until a specified cigarette butt length is reached; if there is a filter overwrap, approximately 10% of the tobacco might be left unburned. However, people smoke more intensively than the smoking machines. For example, data accumulated from 18 studies indicate that on average, smokers take 43-mL puffs at 34-second intervals.[1] Furthermore, when faced with a nominally low-yield cigarette or when faced with limited availability of cigarettes (owing, for example, to smoking restrictions, restricted access to cigarettes, or economic constraints), people smoke cigarettes more intensively to consume an adequate level of nicotine.[4,5,11-13] For example, smokers may take more frequent or deeper puffs or block the ventilation holes with their fingers or lips.[1-5,14]

The discrepancy between cigarette yield ratings and how much nicotine people obtain from cigarettes is explained by the differences between the testing-machine method and how people actually smoke cigarettes. Cigarettes have been designed to reduce machine-testing yields by diluting the mainstream smoke via the use of porous paper and filter ventilation.[15,16] Additional design features include placing less tobacco in each cigarette by using expanded tobacco and/or smaller diameters of cigarettes, shortening the cigarette length, increasing the burn rate of the paper, and increasing the length of the filter overwrap so that the machine is able to take fewer puffs before the cigarette is burned to its specified length.[1,5] However, regardless of their machine-yield rating, all marketed tobacco cigarettes contain approximately 6 to 11 mg of nicotine and enable cigarette smokers to readily extract sufficient levels to produce and sustain dependence.[4,15,16]

Proposed New Rating and Labeling System

We propose a new system of rating and labeling cigarettes. The food-labeling regulations implemented by the FDA in 1994[7] could provide a model for this reformation. Our strategy is summarized in Table 1. An additional strategy that could be used to assist consumers in making informed decisions would be to fully disclose the tobacco smoke constituents of potential health significance, analogous to harmful constitu-

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The views expressed in this article are those of the authors and do not reflect an official position of the federal government or its agencies

Reprint requests to NIDA Addiction Research Center, PO Box 5180, Baltimore, MD 21224 (Dr Henningfield).

Table 1.—Strategies to Provide Meaningful Cigarette Labeling

- Use biologically meaningful categories that have plausible significance with respect to total daily nicotine intake and level of addiction.
- Develop machine-testing parameters based on data relevant to how people smoke and base yield ratings on maximal yields.
- Verify yield ratings with bioavailability testing of cigarette smokers to determine if humans can readily extract more nicotine than predicted by the machine tests.
- Limit the nicotine content of cigarettes in each category to limit maximal nicotine extraction and provide actual content values in the cigarette labeling.
- Link nicotine-rating categories to other factors of toxicological importance, eg, a low nicotine rating would only be permitted if there was also low tar and carbon monoxide delivery.
- Ban the use of terms such as "light" and "ultralight."

ent disclosure for foods.[7]

Our proposal involves categorizing cigarettes based on the amount of nicotine delivered (Table 2). These ratings would be included as part of a new label for cigarettes (Table 3). Developing meaningful categories for cigarettes is somewhat more complicated than for foods because a cigarette is a complex drug-delivery system,[5,17] but the principle is the same. We propose broad categories that should both serve consumer interests[18] and have plausible biological significance. The categories are based on nicotine delivery for two reasons. First, nicotine intake by smokers can be accurately measured. Second, nicotine delivery from cigarettes can be controlled to a maximum limit by controlling the nicotine content of the tobacco. It should be noted, however, that tar and other combustion products of cigarette smoke are believed to be the primary cause of human disease rather than nicotine per se. Unfortunately, it is more difficult to quantitate human tar exposure or to predict tar delivery based on the composition of the cigarette.

Accurate categorization of cigarettes based on their nicotine delivery would also be useful if cigarette manufacturers are ever required to gradually eliminate nicotine from their cigarettes. Cigarettes meeting our criteria of very low nicotine or no nicotine are unlikely to be generally addicting.[14]

We suggest that cigarette descriptors such as "ultralight" and "light" not be allowed. In terms of the food-labeling model introduced earlier, the FDA has limited use of these designations for foods where there is an adequate level of consensus as to the general meaning of the terms and a consensus that products so designated might actually represent generally healthier choices for consumers than the standard products.[7] A similar level of consensus would need to be developed with respect to cigarettes. This may not be possible because terms such as "light" provide connotations that may be interpreted as "beneficial," when, in fact, even exposure to the smoke of a few cigarettes per day has well-documented adverse health effects.[19]

In the reform of food labeling by the FDA, one of the basic issues addressed was to insist that estimates of intake be based on meaningful serving sizes and the number of typical servings taken per day.[7] To this end, machines used to provide estimates of nicotine yield should be programmed with puffing parameters that are representative of the behavior of cigarette smokers. We believe that the actual nicotine content of cigarettes should be included on the label, just as fat content is for food, but such information should not constitute the basis of nicotine-yield categorization. Nicotine content, while providing information on the maximal possible yield, is not reliably predictive of yield when cigarettes are smoked.[2]

Smoking-machine tests should be modified to include the testing of each cigarette under an average smoking condition as well as a heavy smoking condition; in this way, consumers could be informed of the usual and maximal yields of a particular cigarette. The average smoking condition would be a closer approximation to typical smoking than the model currently used. The machines would be programmed to continue puffing until all the consumable tobacco is smoked in filtered cigarettes and until the smallest plausible smokable butt length is reached in nonfiltered cigarettes (eg, 10 mm).

Table 2.—Proposed New Nicotine-Delivery Categories for Cigarette Labeling. Based on Revised Machine-Testing Procedures and Validated by Bioavailability Testing

Cigarette Label	Maximum Nicotine Yield, mg
Nicotine free	0.01
Very low nicotine	0.17
Low nicotine	1.0
Regular	>1.0

Table 3.—Content of the New Cigarette Label

- Warning statement
- Nicotine-yield category
- Nicotine, tar, and carbon monoxide yields (average and maximal)
- Nicotine content
- Harmful additives
- Information about factors affecting nicotine delivery

For cigarettes in which ventilation holes are incorporated, if it is possible for vents to be blocked with the smoker's lips or fingers, then the vents would be occluded in the heavy smoking condition. Ventilation would be incorporated in the test condition only if the ventilation holes were (1) clearly visible, (2) far enough out (perhaps 15 mm) on the filter to discourage easy blocking by the smoker's lips, and (3) described on the package label with a warning to the smoker that blocking the holes would defeat the intent of the product and result in higher levels of exposure to nicotine and other tobacco smoke toxins. Labeling should similarly disclose the sources of nicotine yield variation (eg, puff size and number) and advise how individuals might minimize their intake of nicotine per cigarette.

Cigarettes are, in essence, sophisticated drug-delivery systems,[5,7,15,17] and therefore nicotine bioavailability should be evaluated to verify that human absorption does not exceed levels predicted by the new delivery ratings. Bioavailability testing of smoked drugs is more complex than with conventional drug-delivery systems. The bioavailability of smoked drugs can be affected by parameters both within and outside the control of the user.[1,4,5] However, when factors are known to affect the bioavailability of a drug in a medication, such factors are often noted in labeling and similarly should be noted on cigarette package labels. Bioavailability could be estimated by measuring levels of nicotine, or its metabolite cotinine, in the blood, urine, or saliva of cigarette smokers.[4] Such testing would be important to determine whether alterations in cigarette design affect bioavailability in ways that could affect the categorization of the cigarette.

Although our proposal focuses on nicotine delivery, the model could be applied to other smoke constituents such as tar and carbon monoxide. A precedent for this exists in the reformation of food labeling by the FDA, in which special categories are permitted based primarily on the level of one constituent when another constituent also remains within certain boundaries. Thus, a product high in fat cannot be labeled "cholesterol free," regardless of its cholesterol level.[7] Similarly, we recommend that a cigarette be accorded one of the reduced-nicotine labels only if its tar and carbon monoxide yields are below certain levels. For example, the designation of a cigarette as low nicotine might require that the maximum bioavailability be less than 1 mg of nicotine, 5 mg of tar, and 5 mg of carbon monoxide. Of course, the tar content and carbon monoxide content of cigarettes are not meaningful concepts, because these substances are products of tobacco combustion. However, the ratio of tar or carbon monoxide yield to nicotine yield can be controlled by the design of cigarettes[16,17,20] and may also be useful to include on the label as information to consumers who wish to minimize their exposure to tar and carbon monoxide.

An implication of the present proposal is that few, if any, currently marketed tobacco cigarettes would meet the criteria for a designation other than "regular." To achieve a rating such as "low nicotine," the cigarette would need to be lower in nicotine content, and other design changes involving the use of filters and ventilation holes might be necessitated. It is possible that the proposed rating system would encourage the development of cigarettes useful in helping smokers to lessen their intake of nicotine and other constituents.

Health Benefits

The enhanced labeling system should inform smokers that smoking cigarettes with reduced nicotine yield may facilitate their efforts to quit smoking but may provide little if any general health benefit compared with regular cigarettes. Ultimately, and of greater public health importance, the proposed labeling changes could lessen the prevalence of tobacco smoking. This could come about in several ways. Many consumers are already highly motivated to smoke cigarettes with lower nicotine yield for their presumed health benefits[21]; cigarettes currently labeled "lower yield" (less than 16 mg of tar) account for approximately 60% of the market.[18] If such misleading labeling is prohibited and replaced with an accurate depiction of nicotine yield, health-conscious smokers may be more motivated to attempt to quit. In addition, if manufacturers were to develop and market cigarettes reflecting a broad range of nicotine yields, these products might facilitate the efforts of motivated smokers to effect a gradual nicotine-weaning process. The major goal of improved labeling, however, would be to provide the basic information that can now be obtained with most other consumable products, including alcoholic beverages.

Jack E. Henningfield, PhD
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For Discussion at the Conference on " Alternative Nicotine Delivery Systems: Harm Reduction and Public Health"

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

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

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

I. Basic Principles for Exposure Reduction Products and Strategies

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

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

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

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

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

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

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

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

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

Questions to be Asked of All Indications or Products

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

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

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

3. What are the nicotine delivery characteristics?

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

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

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

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

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

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

10. What level of post marketing surveillance is required?

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

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

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LOW TAR CIGARETTES ARE HAZARDOUS TO YOUR HEALTH

ADVICE FOR SMOKERS

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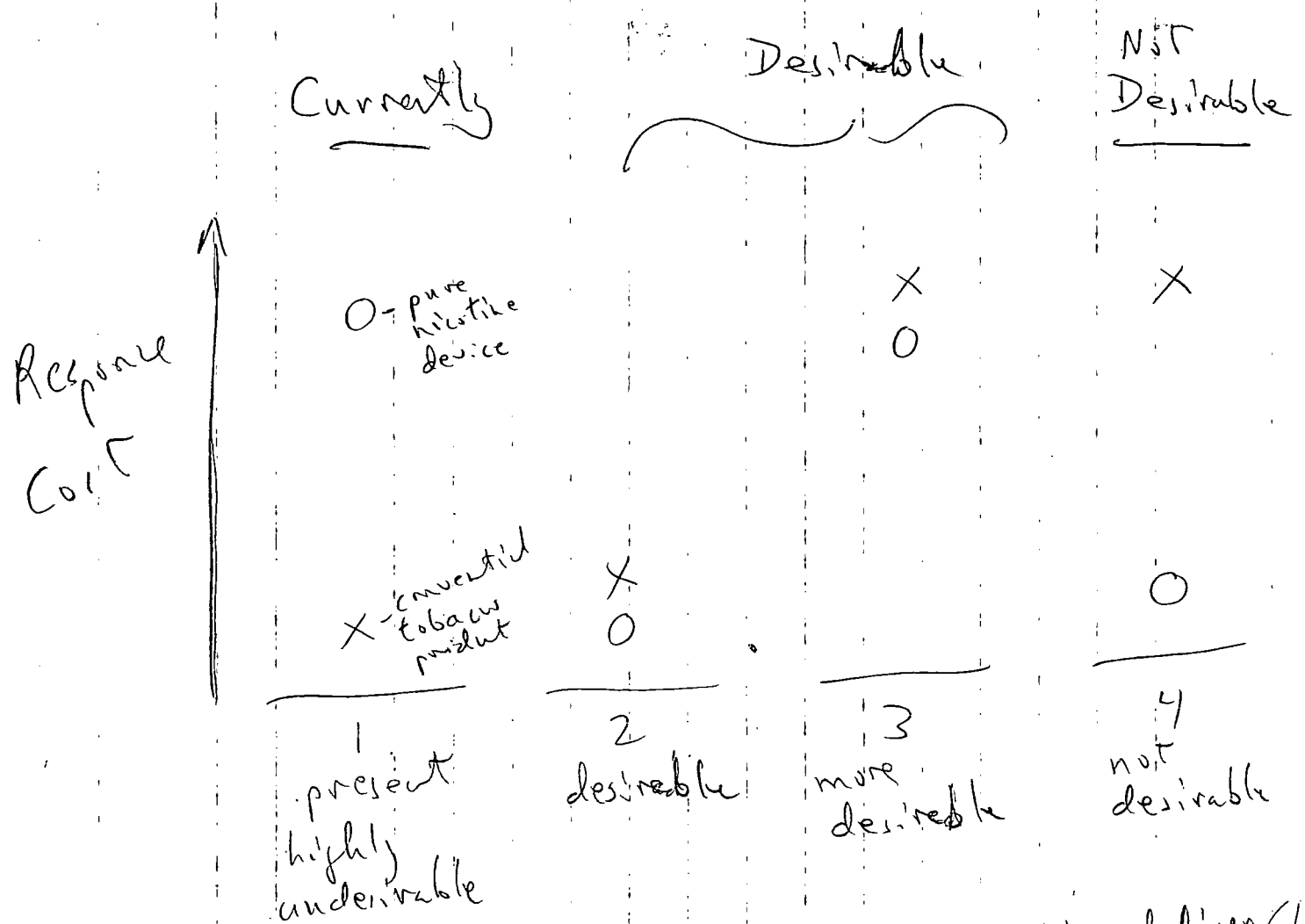

* Response cost = (price, availability, nicotine delivery (bioavailability), taste, ease of use, marketing), packaging, labeling, etc.
→ differential taxa ...

John Slade MD
Robert Wood Johnson Medical School

CEA Draft, July 23, 1997

Incentives to Develop Reduced Risk Products

I. Provisions of the Settlement

Provisions relating to reduced risk products are in Title I, Section E, Part 4. Manufacturers will be required to notify FDA of any technology that they develop or acquire and that reduces the risk from tobacco products and, for a commercially reasonable fee, to cross license all such technology, but only to those companies also covered by the same obligations. Procedural protections will be built in to resolve license fee disputes. If the technology is in the early development stages, manufacturers will be provided confidentiality during the development process. The FDA shall have the authority to mandate the introduction of "less hazardous products that are technologically feasible by requiring the manufacturer who owns the technology (at the manufacturer's election) either to introduce the product or to license the technology to someone who does agree to bring it to market in a reasonable time frame. If no manufacturer or licensee brings such products to market in a reasonable time frame set by FDA, the U.S. Public Health Service may produce the product, either itself or through a licensing arrangement.

The goal "is to guarantee that a mechanism exists to ensure that products which appear to hold out the hope of reducing risk are actually tested and made available in the marketplace and not held back." The economic concern is whether the provisions, especially the cross-licensing requirement, provides an incentive or a disincentive to develop new products.

II. The central economic argument

If innovation occurred spontaneously and irrespective of economic incentives, society's interest would be best served by requiring immediate full disclosure and allowing other firms to adopt new products and technologies without fee. But, as the patent system recognizes, innovation is an economic activity that requires incentives. The fundamental rationale for the patent system is that a) any innovation created by one firm provides usable information to other firms at little or no cost; and b) while all firms stand prepared to use such information, no one firm is willing to pay the sums of money (often huge) necessary to produce it without compensation. The dilemma of the patent system, of course, is that, in encouraging R&D, it discourages diffusion of innovation (see Tirole, *The Theory of Industrial Organization*).

Compulsory licensing shifts the incentives away from encouraging innovation toward encouraging diffusion. It will probably result in less innovation, but it might result in faster dissemination of what does get invented.

III. Analysis

Past innovations aimed at producing safer products have been scant in the tobacco industry, in large measure because to develop and promote safer products would have been to acknowledge

the harm done by existing products. But some innovations, like filters and reduced-tar cigarettes do appear to have followed the appearance of adverse health news about smoking. In the current environment, with companies admitting that their products are harmful and with heightened consumer awareness, individual companies are more likely to view the development of safer products as a profitable endeavor. The patent system, first-mover advantages (the company first on the market with a new product tends to experience enduring marketing advantages), and natural secrecy and imitation lags all increase the inventor's ability to appropriate the financial benefits of developing and introducing safer products and thus increase incentives to devote resources to the effort. Compulsory licensing, by contrast, would discourage this effort. The settlement's requirements for disclosure (that's what a patent does) and mandated introduction of new discoveries are different, however, and do not interfere unduly with incentives to innovate. Moreover, companies can choose to license if they wish, on privately negotiated terms.

IV. Options

1. Maintain compulsory licensing - If all the innovation is already sitting on the shelf.

The current provisions provide limited incentives for innovation but strong incentives for diffusion. This is an acceptable solution if it is thought that most innovation will take place spontaneously or that much knowledge about developing safer products already exists and there is more to be gained from disseminating what is known than from trying to develop new knowledge and new products and technology.

2. Eliminate compulsory licensing but keep disclosure and adoption provisions

This would allow companies to profit from innovation as they would in any other industry, but would greatly reduce incentives for strategic withholding of new innovations. Companies could make money by developing new products but they would not be able to keep them off the market for strategic reasons. Other companies would have incentives to "invent around" patents but rapid diffusion would not be guaranteed. On balance, however, the industry would probably be more technologically dynamic both in developing a stream of new "safe" products and in refining existing products.

3. Provide public "prizes" or awards for the development of safe products (Kessler awards?)

4. Create special patents of a more limited length if existing patent protection is judged to run too long

5. Encourage joint R&D efforts to develop safe products (Sematech?)

6. Publicly fund university research or joint industry-academic efforts to develop safe products

7. Mix & match system - for the next x years one system, switches to another system.
give away what they have now, then move to patent system for future.

PinneyAssociates | *Health Consulting*
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Market Research

July 8, 1997

Jerold Mande
Senior Advisor to the Director
Office of Science and Technology Policy
Old Executive office Building, Room 346
17th Street and Pennsylvania Avenue, NW
Washington, D.C. 20502

Dear Mr. Mande:

Jack Henningfield suggested I write you a brief note to provide additional information on the subject of treatment for tobacco dependence relative to the proposed settlement of the tobacco lawsuits. Jack may have mentioned that there is not very much information available on what treatments are being used, who is using them, and how much they cost. I have enclosed copies of several of our research efforts in this area (some performed under our prior company name Corporate Health Policies Group) and I want to offer to be of any assistance I can in helping you to understand the current state of tobacco dependence treatment in the U.S.

The specific items enclosed are:

- A copy of our 1995 study of smoking cessation in managed care - among the primary findings in this study were that managed care plans take a very low key approach to cessation often characterized by passively offering programs to their general membership, with restrictions and limitations that can discourage participation. Also, since few plans know which of their members smoke, these efforts are necessarily often token at best.
- Our 1996 study of smoking cessation and health promotion in large companies - this study found that many large companies give smoking cessation a relatively low priority due to what they perceive is a lack of interest among smokers; however, most companies offer employees participation in group cessation programs, which are often not convenient or appealing to smokers.
- A copy of an article from the journal *Tobacco Control* that looks broadly at the cessation market and barriers to quitting - among other findings, this article reflects the fact that in many communities, smokers who seek cessation assistance from local community resources often have to wait for long periods before they can access a program.
- An excerpt from an analysis we conducted of the total sales of cessation programs and products, not including what were then prescription nicotine replacement products - this analysis shows that the total market in 1993 was about $85 million, most of which was paid for by individuals and employers. This is a fairly accurate depiction of the very small size of

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the cessation market and suggests that there is enormous room for growth under the proper incentives and with the offer of programs that smokers can easily access and which they find more suitable to the needs.

I believe these and other facts about the rather poorly organized system of care for tobacco dependence need to figure prominently in the way the treatment provisions of the agreement ultimately are resolved. The basic objective to be considered with regard to cessation is to ensure that the settlement results in a coherent national cessation program with appropriate procedures, mechanisms, and modalities so that the maximum number of smokers will receive efficacious treatment. Treatment works, and smokers will avail themselves of treatment that they can afford and that they find accessible and appropriate to their needs. The current success of OTC nicotine replacement products demonstrates this quite well. We as a field and the health care system in general have failed to make treatment a priority and to structure and deliver treatment in ways that smokers can and will access.

One final point bears consideration. The settlement obviously poses a risk of overstimulating an underdeveloped treatment system. Careful thought, along with criteria and standards will be required to avoid this problem. However, this and other problems can be avoided, and the potential effects of a more visible national focus on cessation, combined with a wise strategy for investing whatever funds may flow to treatment, could be the saving of millions of lives that otherwise would end prematurely due to tobacco.

This brief overview cannot serve all your needs for data on the treatment issues. Please feel free to call me at any time if you have questions about the enclosed materials or any other aspect of cessation.

Sincerely,

John M. Pinney
President

cc: Jack Henningfield
John Slade
John Hughes
John Seffrin