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

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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, 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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FAX COVER SHEET

DATE: 7-2-97

TO: Jerry Mander

FIRM:

FAX NUMBER: 202 - 456 - 6027

FROM: John Hughes

NOTES:

This message contains 2 page(s) including this cover sheet.

Fax to Jerry Mande (202) 456-60[redacted]27 from John Hughes

MECHANISM	# GRANTS	$$$$$	
F	8	$109,940	
F31	4	$52,032	Predoctoral Individual National Research Service Award
F32	2	$57,908	Postdoctoral Individual National Research Service Award
K	19	$1,667,234	
K02	2	$207,019	Research Scientist Development Award Research
K04	2	$134,289	Modified Research Career Development Awards
K05	2	$198,212	Research Scientist Award
K07	5	$413,291	Academic/Teacher Award
K08	2	$148,924	Clinical Investigator Award
K11	1	$85,104	Physician Scientist Award (Individual)
K15	1	$57,083	Dentist Scientist Award (Individual)
K16	1	$59,157	Dentist Scientist Award (Program)
K20	1	$135,264	Scientist Development Award for Clinicians
K21	2	$228,891	Scientist Development Award
M01	44	$907,433	General Clinical Research Centers Program
N01	28	$24,735,026	Research and Development Contracts
P	44	$7,664,521	
P01	28	$4,893,867	Research Programs Projects
P30	1	$30,498	Center Core Grants
P41	1	$59,058	Biotechnology Resource Grants
P50	13	$2,539,847	Specialized Center
P60	1	$131,353	Comprehensive Center
R	201	$48,617,161	
R01	157	$43,470,485	Research Project (Traditional)
R03	8	$243,787	Small Research Grants
R18	1	$730,564	Research Demonstration and Dissemination Projects
R29	25	$2,421,173	First Independent Research Support and Transition (FIRST)
R37	2	$598,495	Method to Extend Research in Time (MERIT)
R43	4	$378,901	Small Business Innovation Research Grants (SBIR) Phase I
R44	3	$873,756	Small Business Innovation Research Grants (SBIR) Phase II
R55	1	$100,000	James Shannon Director's Award
S06	1	$86,378	Minority Biomedical Research Support (MBRS)
U	9	$8,400,122	
U01	7	$8,015,502	Research Project (Cooperative Agreements)
U18	2	$384,620	Research Programs (Cooperative Agreements)
Z01	10	$0	NIH Intramural
TOTAL	382	$92,147,812	

AGENCY	# GRANTS	$$$$$	
AA	7	$930,545	N.I. on Alcohol Abuse & Alcoholism
AG	5	$877,308	N.I. on Aging
AI	2	$423,483	N.I. of Allergy & Infectious Disease
CA	73	$22,358,104	N.Cancer I. (NCI)
CB	1	$0	NCI Division of Cancer Biology and Diagnosis
CN	29	$24,298,808	NCI Division of Cancer Prevention and Control
CP	1	$438,219	NCI Division of Cancer Etiology
DA	76	$14,727,806	N.I. on Drug Abuse
DC	1	$38,976	N.I. on Deafness and Other Communication Disorders
DE	9	$765,917	N.I. of Dental Research
DK	1	$66,108	N.I. of Diabetes & Digestive & Kidney Diseases
ES	5	$510,202	N.I. of Environmental Health Sciences
EY	3	$568,317	N. Eye I.
GM	8	$1,703,165	N.I. of General Medical Sciences
HD	4	$550,759	N.I. of Child Health & Human Development
HL	33	$11,455,337	N. Heart, Lung & Blood I
MH	5	$701,482	N.I. of Mental Health
NR	3	$823,767	N.I. of Nursing Research
NS	47	$10,139,946	N.I of Neurological Disorders & Stroke
RR	45	$966,491	N. Center for Research Resources
TW	1	$8,176	Fogarty International Center
TOTAL	382	$92,147,812	

FY95 $ Terms:
nicotine
nicotinic receptor
passive smoking
smokeless tobacco
smoking cessation
tobacco
tobacco abuse
tobacco abuse education
tobacco abuse prevention

N.B.: "smoking" became a term in 1998

Nicotine/Smoking in NIH in 1995

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American Psychiatric Association

Practice Guideline for the Treatment of Patients With Nicotine Dependence

Official Journal of the American Psychiatric Association

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Smoking Cessation

and

Managed Care

1995

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