



Perspective

A Nicotine-Focused Framework for Public Health

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DESPITE EXTRAORDINARY PROGRESS IN TOBACCO CONTROL AND PREVENTION, tobacco use remains the leading cause of preventable disease and death in the United States. Combustible cigarettes cause the overwhelming majority of tobacco-related disease and are responsible for more than 480,000 U.S. deaths each year. Indeed, when used as intended, combustible cigarettes kill half of all long-term users.¹

With the tools provided to the Food and Drug Administration (FDA) under the Family Smoking Prevention and Tobacco Control Act of 2009, the agency has taken consequential steps to prevent sales of tobacco products to children, expand the science base for understanding traditional and newer tobacco products, and conduct public education campaigns. But the agency needs to do more to protect Americans; in

particular, we must shape a regulatory framework that reduces their use of combustible cigarettes. The agency's new tobacco strategy has two primary parts: reducing the addictiveness of combustible cigarettes while recognizing and clarifying the role that potentially less harmful tobacco products could play in improving public health. We must also work toward a greater role for medicinal nicotine and other therapeutic products in helping smokers to quit and remain nonsmokers.

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Evidence shows that most cigarette smokers are concerned about their health and are interested in quitting and that most have tried to quit.² Reducing cigarettes' addictiveness could help addicted users quit more easily and help keep those who are experimenting — young people, in particular — from becoming regular smokers. And the availability of potentially less harmful tobacco products could reduce risk while delivering satisfying levels of nicotine for adults who still need or want it.

The regulatory framework for reducing harm from tobacco must include nicotine — the chemical responsible for addiction to tobacco products — as a centerpiece. Nicotine, though not benign, is not directly responsible for the tobacco-caused cancer, lung disease, and heart disease that kill hundreds of thousands of Americans each year. The FDA's approach to reducing the devastating toll of tobacco use must be rooted in this foundational understanding: other chemical compounds in tobacco, and in the smoke created by combustion, are primarily to blame for such health harms.

Nicotine is, however, responsible for getting smokers addicted to cigarette smoking in the first place — usually while they are children or young adults and their brains are still developing — and keeping them addicted long-term. Combustible cigarettes' efficient method of nicotine delivery means that nicotine inhaled from a cigarette can travel through the lungs and to the brain in less than 10 seconds,³ adding to the addictive potential.

The Tobacco Control Act gave the FDA a regulatory tool called a tobacco product standard that can be used to alter the addictiveness of combustible cigarettes. Standards may be issued to set requirements related to an ingredient or constituent in a tobacco product, or related to any other aspect of product composition, construction, or other property. Establishing the right product standard could alter the addictiveness of combustible cigarettes by setting maximum nicotine levels in these products.

Section 907 of the Food, Drug, and Cosmetic Act authorizes the FDA to establish tobacco product standards that it has determined to be appropriate for the protection of the public health. The statute specifically notes that such a standard may address nicotine yields, among other characteristics. Although it prohibits

the FDA from “requiring the reduction of nicotine yields of a tobacco product to zero,” the agency has clear authority to otherwise reduce nicotine levels.

A nicotine-limiting standard could make cigarettes minimally addictive or nonaddictive, helping current users of combustible cigarettes to quit and allowing most future users to avoid becoming addicted and proceeding to regular use. Disrupting that progression — from experimentation to regular use to tobacco-related disease and even death — could save millions of American lives.

The FDA will consider peer-reviewed studies in proposing a maximum nicotine level. Rigorous studies of very-low-nicotine cigarettes have evaluated the potential effects of various nicotine levels on smoking behaviors and biomarkers,⁴ and findings from such studies could inform decision making on a possible maximum nicotine level in tobacco filler. As on all matters of public health policy, the FDA will be led by the science in this important area.

As we pursue a product standard, the FDA will explore possible adverse effects of such measures, so that any final standard may anticipate and address potential unintended consequences. For instance, compensatory smoking — altering smoking behavior to continue obtaining enough nicotine to satisfy addiction — is a possible countervailing effect of setting a nicotine product standard. Several recent studies have assessed this potential, and some evidence suggests that compensation may be minimal; studies have shown reductions in cigarettes smoked per day and in exposure to harmful constituents.⁴ A recent 6-week study by Donny et al. showed that cigarettes with lower nicotine content reduced nicotine exposure and dependence, as well as the number of cigarettes smoked, as compared with cigarettes with standard nicotine levels.⁵ These results are encouraging, but the FDA will scrutinize all relevant science as part of a transparent, public rulemaking process.

Our assessment of expected population health benefits will also consider the potential for migration — smokers turning to tobacco products other than cigarettes, in combination or as replacements, to maintain their nicotine dependence. Finally, we intend to explore the possibility that regulation might give rise to an illicit market for higher-nicotine products; the FDA will seek input on this issue from experts as we develop our regulatory policy.

With these considerations in mind, and led by the best available evidence, the FDA will pursue a regulatory framework that focuses on nicotine and supports innovation to promote harm reduction. This framework will recognize that the core problem of nicotine lies not in the drug itself but in the risk associated with the delivery mechanism. In contrast to combustible cigarettes, nicotine delivery mechanisms such as medicinal gums, skin patches, or lozenges can be so safe and effective in helping smokers quit that they may be sold without a prescription.

To truly protect the public, the FDA’s approach must take into account the continuum of risk for nicotine-containing products. We are examining possible steps the agency could take to address the pharmacokinetic performance of FDA-approved medicinal nicotine products to help more smokers quit.

Factors for consideration may include the speed with which nicotine is delivered and other possible innovations.

There are already products, such as electronic nicotine delivery systems, that could conceivably deliver nicotine without posing the dangers associated with tobacco combustion. Experts on both sides of the “harm reduction” debate have expressed strongly held views about the potential benefits and risks of e-cigarettes. We must continue to build on our understanding of the potential benefits for addicted cigarette smokers, in a properly regulated marketplace, of products capable of delivering nicotine without having to set tobacco on fire. The FDA’s ongoing investment in regulatory science will contribute to this understanding.

Rendering cigarettes minimally addictive or nonaddictive, within a landscape including other, noncombustible products such as e-cigarettes, represents a promising foundation for a comprehensive approach to tobacco harm reduction. In working toward this vision, the FDA is committed to striking an appropriate balance between protecting the public and fostering innovation in less harmful nicotine delivery.

We are at a crossroads in efforts to reduce tobacco use, with the lives of tens of millions of currently addicted cigarette smokers and future generations hanging in the balance. Even as we evaluate the characteristics of various nicotine-delivery products — and watch the sometimes-divisive debate over these products’ pros and cons — the FDA is focusing squarely on nicotine as the centerpiece of a comprehensive, lifesaving tobacco regulatory strategy. In developing this strategy, we will rigorously assess the best available evidence and provide extensive opportunities for stakeholder input. As a first step, the agency is working on an advance notice of proposed rulemaking to obtain information relevant to reducing the nicotine levels in combustible cigarettes and to ask key questions related to the benefits and potential unintended consequences of such a policy.

The public health benefits of implementing a nicotine-reduction policy for combustible cigarettes could be enormous: we would expect smoking-related morbidity and premature mortality to decrease considerably. Ultimately, we may be able to transform the tobacco marketplace and the delivery of nicotine to protect future generations of young people and save many millions of lives.

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Author Affiliations



Supplementary Material

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Disclosure Forms	PDF	92KB
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Assoc Prof Darlene H Brunzell and colleagues ▾

Sep 27, 2017

Nicotine, not just about the addiction

We agree with the overwhelming need to decrease cigarette consumption, but are concerned about labeling various nicotine products and alternative delivery systems as 'so safe.' It is difficult, to fully disentangle the harm done by nicotine versus the other toxic constituents in tobacco. Nicotine is a known carcinogen, toxin and teratogen. Preclinical studies show that nicotine promotes tumor growth and GWAS studies show that some nicotinic receptor variants increase cancer vulnerability. While e-cigarettes can help some smokers to quit, e-cigarette use encouraged by youth-targeted marketing is rapidly increasing in never-smoker adolescents who report starting e-cigarettes because they are viewed as "safer" than conventional cigarettes. There is growing evidence that e-cigarettes encourage cigarette consumption in these youth and there are conflicting claims about the health concerns posed by e-cigarette vapors. As we work together to reduce tobacco's toll, we should take great care in crafting messages about nicotine; otherwise we may inadvertently spur chronic use and perpetuate some of tobacco's harms.

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RAMAKRISHNA PINJALA [✉]

Sep 21, 2017

Is it possible to stop production of combustible cigarettes?

It is still a challenge, but I feel behavioural therapy is essential to overcome the addictions. Reduction of nicotine levels will help many, but there is concern about the possibility of smoking more to get the same effect. Combustible cigarettes production should be stopped, this will help the non smokers. Alternatives can be provided for some time, such as e-cigarettes.

AKI NILANGA BANDARA [✉]

Sep 21, 2017

Smoking cessation and harm reduction

I read with interest a recent article by Gottlieb and Zeller (1). Even though the authors have explicitly stated that there is growing evidence to support e-cigarettes and it's effectiveness and safety for smoking cessation and harm reduction, unfortunately this statement does not reflect the current best evidence. Best evidence includes empirical evidence from methodologically strong systematic reviews.

There is currently little evidence on the long-term benefits or harms of e-cigarette. According to the FDA, there's no evidence any e-cigarette is safe and effective at helping smokers quit. E-cigarette contains nicotine, which is addictive in itself and therefore, we should not promote these products until the evidence is clear on their efficacy and safety. Therefore, clinicians and the public health community must direct their patients, those who wanted to quit tobacco to other proven and safe tobacco cessation products such as nicotine gum

and patches. E-cigarette is strictly regulated in many countries due to advice from the World Health Organization (WHO), exclusively based on currently available best evidence.

BRIAN MCMILLEN 
Sep 21, 2017

Nicotine sets the taste

The authors seem to be unaware of the role of nicotine in setting the taste of a cigarette for the smoker. The "Tobacco Papers" revealed that the tobacco industry knew that a cigarette was a unit dose of nicotine and that the amount of nicotine set the taste. Before varenicline (Chantix) there was mecamylamine, a ganglionic blocker that entered the central nervous system. Smokers that received a dose of mecamylamine who then inhaled from their favorite brand of cigarette would complain that the cigarette did not taste good. When Phillip-Morris came out with their Marlboro brand, it quickly knocked out the competition and the other companies were at a loss as to why. Turned out, the tobacco had been fumed with ammonia that allowed greater release of nicotine when smoked: i.e. better taste.

What we are observing in the 2015 reports from both the CDC's Youth Risk Behavior Surveillance system and Monitoring the Future is a large drop off in consumption of cigarettes by youth with a compensatory increase in e-cigarettes and vaporizers. Instead of burnt plant products, they are getting a potpourri of flavorings.

In sum, we need to address the behaviors.

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