



Perspective

A Nicotine-Focused Framework for Public Health

Scott Gottlieb, M.D., and Mitchell Zeller, J.D.

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.

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 reg-

ulated 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, life-saving 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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From the Office of the Commissioner (S.G.) and the Center for Tobacco Products (M.Z.), Food and Drug Administration, Silver Spring, MD.

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