On March 16, 2018, the U.S. Food and Drug Administration (FDA) issued an Advance Notice of Proposed Rulemaking (ANPRM) to obtain information “for consideration in developing a tobacco product standard to set the maximum nicotine level for cigarettes.”

This is the signature element of the agency’s new regulatory plan for tobacco products. An aggressive product standard from the FDA rendering cigarettes non-addictive is a critical step towards eventually ending the death and disease inflicted by tobacco products.

Because this standard has such tremendous potential to drastically change the market for combustible cigarettes in the United States, public health stakeholders must engage fully in the process by presenting the evidence base for comprehensive rulemaking and encouraging the FDA to establish rules that are the most protective of the public’s health. This will be a long process; the first step in that process is commenting on this ANPRM.

Unlike traditional academic writing, the FDA expects comments to be persuasive and is specifically soliciting this information to inform its rulemaking process. This may feel unfamiliar and
even uncomfortable for public health scientists and researchers, but it is important to convey your view to the FDA. Even preliminary but informative evidence that supports the protection of public health can help in the process of shaping a comprehensive nicotine standard.

Additionally, federal rulemaking is a long process measured in years rather than days or months. Because of this, researchers can also see the FDA’s questions as potential gaps in the scientific knowledge that could be answered through modifying existing projects or aims (for example, adding questions to a survey) or that could be addressed in future grant proposals. Scientists should share with the FDA any new research or data that is developed on this topic, even after the end of the comment period.

It is particularly important to tell the FDA that:

- The existing evidence base strongly supports FDA action to reduce nicotine in combustible products.
- Given the millions of lives that are at stake, the FDA needs to finalize this regulation as soon as possible.
- A comprehensive nicotine standard must address all combustible tobacco products: cigarettes, all cigars, so-called “heat-not-burn” products, waterpipe tobacco, roll-your-own tobacco, and pipe tobacco.
- The FDA should quickly implement a standard for combustible products that lowers nicotine to sub-addictive levels and also implement a standard for noncombustible products that gradually lowers nicotine to sub-addictive levels over a period of years.

Submit relevant information even if the FDA has not specifically asked for it.

Unlike a Notice of Proposed Rulemaking, which solicits comments on the language and content of a proposed rule, an ANPRM allows an agency to gather information about a topic to inform a future FDA rule. In this case, the public health community has an opportunity to shape the FDA’s proposal before it is written. The FDA is gathering scientific evidence, field research, and other useful information that will assist the agency in determining the scope of a future product standard and the best way to implement and enforce such a standard. The agency’s questions from the notice are compiled and categorized below. Consider answering these questions as you draft and submit your comment.
Scope of the Standard

FDA Question
If FDA were to propose a product standard setting a maximum nicotine level, should such a standard cover other combusted tobacco products in addition to cigarettes? If so, which other products? If FDA were to propose to include additional categories of combusted tobacco products in a nicotine tobacco product standard, should the standard be tailored to reflect differences in these products? What criteria should be used to determine whether, and which, products should be covered?

Our Take
The FDA absolutely must set a maximum nicotine level that covers all combusted tobacco products. This should also include emerging products like heated cigarettes (iQOS, glo, Revo, etc.).

FDA Question
Some suggest that large cigars and those cigars typically referred to as “premium” cigars should be regulated differently from other cigars, asserting that they are used primarily by adults and their patterns of use are different from those of regular cigars (81 FR 28973 at 29024). FDA requests information and data on whether large and/or so-called premium cigars should be excluded from a possible nicotine tobacco product standard based on asserted different patterns of use, and whether large and/or so-called premium cigars would be migration (or dual use) candidates if FDA were to issue a nicotine tobacco product standard that excluded premium cigars from its scope. FDA also requests data and information on whether and how there is a way that, if FDA were to exclude premium cigars from the scope of a nicotine tobacco product standard, FDA could define “premium cigar” to include only unlikely migration or dual use products and thereby minimize such consequences.

Our Take
The FDA's recent decision to deem and begin regulating premium cigars was based on its finding that “(1) All cigars pose serious negative health risks, (2) the available evidence does not provide a basis for FDA to conclude that the patterns of premium cigar use sufficiently reduce the health risks to warrant the exclusion, and (3) premium cigars are used by youth and young adults.” Because those findings remain accurate, the agency must continue to regulate so-called premium cigars in a manner that is consistent with the evidence and best protects public health.
FDA Question
Should waterpipe tobacco products, which are different from regular pipe tobacco, be included in such a standard? Are there data showing different use topographies or that they are not likely to be migration substitutes or dual use candidates? If FDA were to issue a nicotine tobacco product standard that did not include waterpipe tobacco products within the scope, what would be the likelihood that former smokers would switch to waterpipe tobacco to maintain their nicotine addiction? What are the relative risk consequences of switching to waterpipe tobacco?

Our Take
Evidence shows that the health harms of waterpipe tobacco are often equivalent to or exceed the health harms of combustible cigarettes, necessitating that these products be subject to the same product standards as other combustible products.

Maximum Nicotine Level

FDA Question
The Family Smoking Prevention and Tobacco Control Act prohibits FDA from reducing nicotine yields in any combusted tobacco product to zero (section 907(d)(3) of the FD&C Act). If FDA were to propose a maximum nicotine level for cigarettes, what should be the maximum level to ensure that the product is minimally addictive or nonaddictive, using the best available science to determine a level that is appropriate for the protection of the public health? Rather than establishing a nicotine target to make products “minimally addictive” or “nonaddictive,” should FDA consider a different threshold (e.g., less addictive than current products on the market)? How should the maximum level be measured (e.g., nicotine yield, nicotine in cigarette filler, something else)? What would be the potential health impacts of requiring a maximum nicotine level such as 0.4 mg nicotine/g of tobacco filler? FDA is interested in public health impacts of requiring different maximum nicotine levels, such as 0.3, 0.4, and 0.5 mg nicotine/gram of tobacco filler, as well as other maximum nicotine levels and solicits comments about the potential health impacts of different maximum levels.

Our Take
To be the most protective of public health, the FDA should establish a maximum nicotine standard that is nonaddictive. A product standard that maintains some addiction level, even minimally, will not achieve the maximum benefit to public health.
FDA Question
FDA lists four types of studies to estimate the threshold of nicotine addiction (i.e., indirect estimates; findings of increased cessation for VLNC cigarettes; subjective effects, craving, and withdrawal associated with VLNC cigarettes; and lower nAChR occupancy and cerebral response from the use of VLNC cigarettes). Should FDA rely on some or all of these types of studies? Why or why not? Is there a different method that FDA should investigate or use to determine the threshold for nicotine addiction?

FDA Question
In addition to nicotine, minor tobacco alkaloids (including nornicotine, cotinine, anabasine, anatabine, and myosamine) and tobacco smoke aldehydes (such as acetaldehyde) are pharmacologically active and may contribute to addiction (see, e.g., Refs. 98 and 99). Researchers have investigated the abuse potential of nornicotine, cotinine, anabasine, and acetaldehyde in animals (Ref. 100). However, many of these compounds are only present in tobacco smoke at low levels and are likely less potent than nicotine in mediating pharmacological response and, therefore, reinforcement (Refs. 101 and 102). In addition to setting a maximum nicotine level, should the product standard also set maximum levels of other constituents (e.g., nornicotine, acetaldehyde, anabasine) that may have the potential to produce dependence and be addictive? If so, at what levels?

Our Take
Unlike nicotine, the FDA has the authority to establish product standards for other constituents in tobacco that prohibit them entirely. To be the most protective of public health, as much as it is feasible, the FDA should reduce any potentially addictive constituents to zero or to non-addictive levels.

FDA Question
If FDA were to finalize a nicotine tobacco product standard, what is the potential that adults and adolescents would perceive these VLNC cigarettes as “safe”—and how could youth and adult risk perceptions of these cigarettes impact initiation, use, and cessation habits of combusted tobacco products?
Our Take

Potential tobacco product users, especially youth, are targeted heavily through marketing and the labeling of products. To counteract the industry’s aggressive targeted marketing, the FDA should take the critical steps of requiring graphic warning labels and stringently enforcing the prohibition on modified risk claims against all products. The FDA should also take the concurrent step of prohibiting flavors in all tobacco products. Finally, the FDA should prevent newly non-addictive cigarette manufacturers from making modified risk claims.

Implementation (Single Target vs. Stepped-Down Approach)

FDA Questions
What data are available to demonstrate that a single target approach to reach a maximum nicotine level would or would not result in any unintended consequences?

In the alternative, what data are available to demonstrate that a stepped-down approach involving a sequence of incremental levels and implementation dates to reach a proposed nicotine level would or would not result in any unintended consequences?

If FDA were to select a stepped-down approach for a nicotine tobacco product standard, what scientific evidence exists to support particular interim nicotine levels and the appropriate number of steps that would be needed to reach the target level?

Would a single target and a stepped-down approach for implementation result in comparable quit rates or reduced initiation rates?

What would be the likely implementation differences, including implementation timelines and transition costs, between a single target approach or a stepped-down approach involving a sequence of incremental levels and implementation dates?

Our Take
Every FDA action should be the option that is most protective of public health, and scientists should submit evidence to support a single target approach. The FDA should also propose a rule that would address any unintended consequences of such an approach. For example, the FDA should implement a track and trace program to reduce illicit trade.
Analytical Testing Method

FDA Question
If FDA were to issue a product standard, should the Agency require a standard method of product testing to analyze the nicotine levels in products subject to the standard? If so, what method or methods should FDA use?

Should the Agency require manufacturers to sample their products in a specific manner to ensure that products do not contain excess levels of nicotine? Should manufacturers be required to test each manufactured batch to ensure compliance with a product standard limiting nicotine levels? What criteria should be used to determine if a batch passes or fails testing?

Our Take

The FDA should use a standard method that does not solely rely on manufacturers’ testing and reporting. Tobacco industry manufacturers have a long history of manipulating testing to maintain their profits. Whether or not the FDA requires a manufacturer to also test their products, the FDA must implement an independent, scientifically robust method of ensuring that final products have non-addictive levels of nicotine and other addictive constituents.

Technical Achievability

FDA Question
What methods are tobacco product manufacturers currently using to maintain consistency of the nicotine in their products, given the variability of nicotine levels over growing seasons and crop type? How could these methods be adapted to ensure that certain combusted tobacco products meet a potential nicotine tobacco product standard?

What is the feasibility of using the techniques discussed in this section, or other nicotine reduction techniques, to reduce the nicotine in cigarettes?

What is the feasibility of using the techniques discussed in this section, or other nicotine reduction techniques, for non-cigarette combusted tobacco products (e.g., cigarette tobacco, RYO tobacco, little cigars, large cigars, cigarillos, pipe tobacco, and waterpipe tobacco) that FDA is considering covering under a nicotine tobacco product standard?

If FDA were to propose a tobacco product standard setting a maximum nicotine level, how, if at all, would such a product standard impact tobacco farmers’ growing and/or curing practices? If
FDA were to finalize a nicotine tobacco product standard, what would be the costs and benefits for tobacco farmers and tobacco processors, particularly regarding how any such rulemaking might affect them in light of new technologies and business opportunities that are foreseeable, but not now in place? In addition, if FDA were to finalize a nicotine tobacco product standard, what would be the costs for farmers in light of such a standard?

Section 907(d)(2) of the FD&C Act provides that a tobacco product standard must set forth the effective date of the standard, which may not be less than 1 year after publication of a final rule unless FDA determines that an earlier effective date is necessary for the protection of the public health (and that such effective date be established “to minimize, consistent with the public health, economic loss to, and disruption or dislocation of, domestic and international trade”). This section also provides that the effective date be a minimum of 2 years after publication of a final rule if the tobacco standard can be met only by requiring “substantial changes to the methods of farming the domestically grown tobacco used by the manufacturer.” Therefore, if FDA were to propose a product standard setting a maximum nicotine level, when should this standard become effective? What implementation timeframe would allow adequate time for industry to comply? Should the same timeframe be required for all tobacco product manufacturers, regardless of their number of employees and/or annual revenues?* Given the currently available processes to reduce the nicotine in tobacco products (e.g., chemical processes, genetic engineering), what do manufacturers and others with relevant expertise consider an appropriate timeframe to implement a product standard to reduce nicotine? Would a 2-year, 4-year, or 6-year timeframe be appropriate?

**Our Take**

The FDA has identified several methods for adjusting the level of nicotine in tobacco that either happens pre-farming (genetic modification) or post-farming (chemical extraction) and it cites evidence to support the feasibility and affordability of such processes. Because the FDA should not delay this product standard, the FDA should seek to require methods of nicotine reduction that could be implemented quickly.

**FDA Question**

Should the standard include provisions that would allow manufacturers, distributors, or retailers to sell off existing nonconforming inventory of manufactured combusted tobacco products? If so, what would be a reasonable sell-off period?

* The Tobacco Control Act defines “small tobacco product manufacturer” to be a tobacco product manufacturer that employs fewer than 350 employees (21 U.S.C. 387(16)). In the preamble to the deeming rule, FDA defined “small-scale tobacco product manufacturers” to be a manufacturer of any regulated tobacco product with 150 employees or fewer and annual total revenues of $5 million or less (81 FR 28973 at 28980). If you are providing comments or information relevant to these definitions or a different definition, please note that definition in your comments.
Our Take

The FDA should not establish a sell-off period for non-compliant products. The agency’s decision-making must be guided by the public health standard, which compels the agency to prioritize health over the manufacturers’ profits.

FDA Question
What are the potential outcomes of implementing methods to reduce nicotine content in cigarettes in terms of impact on characteristics of cigarettes (flavor, taste, aroma, etc.) and user experience?

Our Take
Because the best public health outcome is to make the user experience undesirable and encourage cessation, any negative effects on flavor, taste, aroma are a positive result.

Possible Countervailing Effects

FDA Question
In addition to a nicotine tobacco product standard, should FDA consider any additional regulatory action to address the possibility of migration to, or dual use with, other tobacco products?

Our Take
Ending tobacco addiction should not stop with combustible products; a comprehensive approach to nicotine addiction requires a nicotine product standard that applies to all tobacco products.

FDA Question
If FDA were to issue a product standard setting a maximum nicotine content for cigarettes, would smokers seek to add liquid nicotine to their VLNC cigarettes? Therefore, should such a regulation include provisions prohibiting the sale or distribution of any tobacco product designed for the purposes of supplementing the nicotine content of a combusted tobacco product (or any product where the reasonably foreseeable use is to supplement this nicotine content)? How could such a provision be structured to efficiently and effectively achieve this purpose?
Should FDA consider other means to prevent supplementing the nicotine content of a combusted tobacco product subject to a nicotine tobacco product standard?

Our Take

The FDA should take steps to ensure that products created solely to circumvent this standard are prohibited.

FDA Question

Would a nicotine tobacco product standard affect the current illicit trade market, and, if so, to what extent? How would users obtain their sources of tobacco in an illicit market? How would manufacturers distribute their illicit products and develop consumer awareness of such products? How would such sales take place?

Our Take

The FDA should implement a track and trace program to mitigate the effects of illicit markets.

FDA Question

FDA hypothesizes that, based on currently available research, nicotine levels like those levels that FDA would consider with a possible nicotine tobacco product standard would be self-limiting (i.e., smokers would be unable to obtain their nicotine dose from cigarettes no matter how they smoke them and eventually would stop trying to do so). Do any peer-reviewed studies demonstrate that lowering the nicotine content of cigarettes to minimally addictive levels might encourage consumers to smoke more VLNC cigarettes to achieve the higher nicotine doses currently delivered by NNC cigarettes?

If a nicotine tobacco product standard were in effect, the following outcomes could occur: (1) Smokers could continue to smoke but use the low nicotine products; (2) smokers could completely switch to, or dual use low nicotine products with, other legal tobacco or nicotine products; (3) smokers could quit using any nicotine or tobacco product; or (4) smokers could seek to buy illegal cigarettes in an illicit market. Are there data that would provide information on which of these outcomes is most likely? Is there some other outcome that could occur?

If an illicit market developed, what percentage of current smokers would switch to illicit conventional cigarettes rather than quitting or switching to other legal products? How would this
change if illicit conventional cigarettes were more expensive and/or harder to obtain? How would this change with the implementation of improved monitoring and enhanced enforcement by FDA and its partners?

If a nicotine tobacco product standard prompted growth of an illicit market, how long would it likely last? Would demand likely decrease over time, stay the same, or increase?

If a nicotine tobacco product standard prompted growth of an illicit market, what effect, if any, would this have on the market for illegal drugs? Are there data showing a relationship between illicit tobacco use and illegal drug use?

What mechanisms may be used to prevent, control, or contain illicit markets in conventional cigarettes that may develop if FDA establishes a product standard? What State and Federal entities may be responsible for these mechanisms, and how much would they cost?

**Our Take**

The FDA should develop a track and trace program to mitigate the effects of illicit markets.

**Other Considerations**

**FDA Question**

What data may be helpful to assess the universe of tobacco products that are currently available to consumers and their relevant characteristics, such as nicotine levels? How can available sources of information, such as manufacturer registrations and/or product listings with FDA, be used in this assessment?

How should potential consumer surplus or utility loss from the removal of nicotine in cigarettes be considered, given the availability of other sources of nicotine such as ENDS and the continued availability of combustible tobacco products?

**Our Take**

In the past, the FDA has used the concept of consumer surplus to overvalue the lost pleasure to smokers as a result of its actions. This runs contrary to our understanding of addiction because it is well known that most smokers want to quit.
FDA Question
What sources of information could be used to estimate the change in demand for VLNC cigarettes? What factors should we consider in estimating the changes in demand for other tobacco products?

What factors should be considered in estimating changes in experimentation and initiation that may occur as a result of a potential nicotine tobacco product standard?

In what ways might a change in nicotine levels in cigarettes spur innovation in the market for both combusted and noncombusted tobacco products?

What factors should be considered in estimating the impacts of externalities that might exist for VLNC cigarettes, such as secondhand smoke, litter, and pollution? How could the impact of externalities for VLNC cigarettes be compared to the impacts from NNC cigarettes?

What factors should we consider in estimating the impact of changes in demand for other tobacco products?

If FDA were to finalize a nicotine tobacco product standard, what might be the costs to current smokers?

Are there any other relevant comments or information that would be helpful for FDA to consider in analyzing the economic impacts of a proposed nicotine tobacco product standard?

Researchers preparing comments can reference the Public Health Law Center’s publications Getting Scientific Research to the FDA and Telling the Public Health Story to the FDA.

Visit the Public Health Law Center’s FDA Action Center for the latest developments related to the FDA’s regulation of tobacco products, including additional information on the nicotine ANPRM.

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