Comments to FDA on the Premarket Tobacco Product Applications Proposed Rule

December 16, 2019

Admiral Brett M. Giroir, MD
Acting Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: Docket No. 2019-N-2854, Premarket Tobacco Product Applications and Recordkeeping Requirements

Dear Acting Commissioner Giroir:

The American Lung Association and the American Thoracic Society are pleased to submit these comments to Docket No. 2019-N-2854, the proposed rule for Premarket Tobacco Product Applications and Recordkeeping Requirements.

The American Lung Association is the oldest voluntary public health organization in the United States and is committed to eliminating tobacco use and tobacco-related disease. Tobacco use is the leading cause of preventable death and disease in the United States, killing 480,000 Americans each year and another 16 million Americans live with a tobacco-caused disease.

The American Thoracic Society (ATS) is a medical professional society with over 16,000 members dedicated to the prevention, detection, treatment and cure of respiratory disease, critical care illness and sleep disordered breathing. The ATS pursue this mission through research, education, clinical care and advocacy. As experts in respiratory health, we are keenly aware of the death and disease caused by tobacco use.

The American Lung Association and the American Thoracic Society shared goal is an end to the use of all tobacco products. Preventing the loss of another generation to tobacco products must be FDA's top priority. As such, we believe that any actions FDA takes must first be aimed at preventing youth initiation of tobacco products. After youth, FDA must next prioritize all tobacco users who are ready to end their use of all tobacco products. At present, evidence on e-cigarettes is insufficient to demonstrate they can be marketed without appealing to children or without resulting in their use in conjunction with combustible tobacco.

This rule must accomplish two essential objectives. First, it must effectively implement the premarket review authority granted to the FDA by the Tobacco Control Act in a way that is faithful to the requirements of the statute. Second, it must establish a regime for premarket review that effectively addresses the crisis of tobacco use that has been fueled by the absence of premarket review. The elements of this crisis are clear:

- There is an epidemic of youth usage of e-cigarettes. In the past two years there has been a 135 percent increase in youth use of e-cigarettes.[1] Moreover, frequent usage by youth—an indication of addiction—has risen alarmingly. Thus, despite a reduction in youth cigarette smoking, overall youth usage of tobacco products has risen.

- Despite an ostensible prohibition on the introduction of new tobacco products since August 8, 2016, e-cigarette products have become far more addictive. Thousands of more addictive new products have been introduced and many others have been modified to deliver nicotine in more addictive doses.

- There is no persuasive scientific evidence that e-cigarettes have contributed to a reduction in adult smoking. Rather, the evidence shows that many smokers who use e-cigarettes are dual or poly-tobacco product users who derive no substantial health benefit from e-cigarette usage and that many young adults who have never before used tobacco products have used e-cigarettes to initiate tobacco use, including traditional cigarettes.

- The ability to market e-cigarettes without premarket review has discouraged manufacturers from pursuing authorization for more effective tobacco cessation products and encouraged irresponsible marketing of products that have not been shown to provide any health benefit.

A large number of the products that are likely to be the subject of PMTAs in 2020 have been on the market for more than three years and a substantial body of information about their advertising, marketing, production and use known by manufacturers. In evaluating PMTAs for these products, it is vital that FDA require comprehensive production of all this information for the entire period during which such products have been sold. Inexplicably, the proposed rule fails to require production of such information. FDA cannot properly fulfill its statutory obligation to protect the public health unless this glaring defect is corrected.

The Proposed Rule Must Be Consistent with The Requirements of the Tobacco Control Act

The requirement of premarket review for new tobacco products is one of the most important provisions of the Tobacco Control Act. FDA's obligation to conduct premarket review is mandatory and the standards under which such review must be conducted are established by the statute. The statute directs FDA to deny an application to market a new tobacco product

unless the manufacturer demonstrates, by scientific evidence, that the marketing of the product is "appropriate for the protection of the public health" and provides that:

"…appropriate for the protection of the public health shall be determined with respect to the risks and benefits to the population as a whole, including users and nonusers of the tobacco product, and taking into account—

A. the increased or decreased likelihood that existing users of tobacco products will stop using such products; and
B. the increased or decreased likelihood that those who do not use tobacco products will start using such products."[2]

The statute requires that the manufacturer of a new tobacco product bear the burden of establishing each element of the statutory requirement. As stated by the United States Court of Appeals for the District of Columbia in its recent decision upholding the validity of the premarket review provisions of the Deeming Rule,

> "The premarket approval requirement is in the Act. It was Congress, not the FDA, that imposed it on new tobacco products, including e-cigarettes. There is no exemption in the Act for certain new tobacco products speculated to be less risky than other new tobacco products. Only tobacco-products consistent with the population-level effects standard fulfill the Act's requirement that each new tobacco product's risks not outweigh its benefits to the public health. Once the FDA deemed e-cigarettes to be 'tobacco products'. . .e-cigarettes became subject to premarket authorization and the requirement to meet the public health standard. The FDA is not authorized to deviate from this statutory standard."[3]

FDA's obligation is clear. The burden of proving each and every element of meeting the public health standard is on the manufacturer. Each element must be proved by scientific evidence. Moreover, each individual product must satisfy this standard. A showing that e-cigarettes in general or even certain e-cigarette products *may* provide a public health benefit is not sufficient to establish that another e-cigarette product satisfies the standard.

The proposed rule is generally consistent with these requirements. Our organizations strongly urge FDA to maintain these requirements in the final rule, to resist suggestions that they be altered to mitigate their effects, and to enforce them strictly in practice.

The Final Rule for PMTAs Must Address the Crisis of Tobacco Use That Has Arisen Since the Deeming Rule was Promulgated.

Although it is essential for the final PMTA rule to be consistent with the statutory standards, it must also address the crisis of tobacco use that has arisen since the Deeming Rule was promulgated. In large part, this crisis has arisen as a result of new tobacco products that are likely to be the subject of PMTAs and any final PMTA rule must be structured to address them. In fact, if FDA fails to establish an effective regime for evaluation and enforcement of

PMTA requirement, it will be impossible for FDA to protect the public health as the statute requires it to do.

The most important aspect of this crisis is the epidemic of youth usage of e-cigarette products and establishing an effective PMTA regime to address this problem must be FDA's highest priority. To the extent that young people are using and becoming addicted to products that will be the subject of PMTAs, the PMTA process must be designed to protect them against such products. And to the extent that young people are using and becoming addicted to products for which PMTAs are not filed, FDA must institute enforcement to remove such products from the market and do so promptly.

The fact that attacking the youth epidemic is by far the most important problem the PMTA process must address does not mean that it is the only significant problem. In addition to the problem of youth addiction to e-cigarette products, the PMTA process must be properly designed to evaluate the extent to which new tobacco products are influencing or are likely to influence adult tobacco use.

Unfortunately, it appears that a substantial portion of adult usage of e-cigarette products does not contribute to the complete cessation of tobacco use. Evidence indicates that a substantial number of adult e-cigarette users are dual or poly-users of tobacco products, a status that provides no health benefit and a new study found that dual use increases the risk for lung disease.[4] Although it has been suggested that such dual users may be in the process of transitioning to giving up smoking, manufacturers must be required to provide evidence regarding the presence of dual or poly-use and the degree to which such dual or poly-use is in fact transitional to tobacco use cessation. The final rule should make it clear that such evidence is required.

Furthermore, there is evidence that a substantial portion of adult usage of e-cigarette usage is by adults who have never used tobacco products. Such usage does not confer any public health benefit and, to the extent that it occurs it provides no counterweight to the detriment caused by youth usage.

In addition, it is important to ensure that PMTA products do not decrease total net cessation. Switching from one tobacco product to another is not cessation. We know that 68 percent of cigarette smokers desire to quit[5] and we know that adult cigarette smoking prevalence is at an historic low of 13.7 percent.[6] No PMTA authorized product should undermine this public health progress. As such, PMTAs should be required to demonstrate that a PMTA product's marketing will not undermine adult smokers desire to quit and post-market surveillance must show that the product does not undermine or reduce total tobacco cessation.

Finally, and importantly, in establishing a final PMTA rule FDA should give careful consideration to the effect the PMTA pathway has on the development of smoking or nicotine cessation products that can be shown to be safe and effective and that can achieve approval under Title V of the Food. Drug and Cosmetic Act.

In the absence of premarket review, manufacturers of e-cigarettes have made unauthorized, unverified, and illegal claims about the ability of their products to enable smokers to quit smoking. On May 9, 2019, a coalition of major public health groups, including the American Lung Association, sent a letter to FDA detailing therapeutic claims made by Juul Labs for its products.[7] In September, 2019, after prodding from the U.S. House of Representatives Oversight and Reform Committee and public health groups, FDA issued a letter to Juul Labs ordering it to desist from making unauthorized modified risk claims about its products.[8] Unlike the manufacturers of nicotine replacement treatment or NRT products, who have had to substantiate their claims in a rigorous scientific process, e-cigarette manufacturers have made such claims, explicitly or impliedly, for years without FDA review and approval.

After youth, FDA must next prioritize all tobacco users who are ready to end their use of all tobacco products. Regulatory policies should promote the use of treatments indicated for smoking cessation approved by FDA's Center for Drug Evaluation and Research (CDER) as the gold standard option for current smokers. FDA should also prioritize and encourage the development and approval of new CDER-approved quit smoking products, including products to enable youth cessation. PMTA authorized tobacco products must never be viewed as an alternative or replacement for safe and effective tobacco cessation treatments approved by FDA. Development of an appropriately rigorous PMTA process will contribute to this goal and facilitate policies designed to achieve the goal of ultimately ending the use of all tobacco products.

Addressing the Youth Epidemic

At least three elements have significantly contributed to the epidemic of youth e-cigarette usage: the advertising, marketing and promotion of these products; the availability of flavors; and the vastly increased abuse liability of products containing nicotine salts. The final PMTA must require manufacturers to submit sufficient information to permit FDA to address each of these key elements.

1. <u>Advertising, Promotion and Marketing and the Demographics of Usage and Use Topography.</u>

As described in detail in the comments filed by public health organizations in this docket, the advertising, promotion and marketing of e-cigarette products to youth has greatly contributed to the youth e-cigarette epidemic and effectively addressing the epidemic requires FDA to prevent such activity in the future and to take proper account of the effect of past actions in evaluating PMTAs. One of the most important flaws in the proposed rule is FDA's failure to require submission of comprehensive information regarding the advertising, promotion and marketing of products that are the subject of PMTAs. Provision of this information is essential for FDA to appropriately evaluate a PMTA.

As noted in the comments of the some of the other public health organizations, the proposed rule does require appropriate information regarding advertising, promotion and marketing as part of Post-Market Review. The final rule should require provision of precisely the same information for all periods during which the product has been advertised, promoted and marketed.

Moreover, as also noted in the comments of the Public Health Organizations, full information of product sales, the demographics of users as well as the topography of usage must be required for the entire period during which the product has been sold.

2. Flavors

An important contributor to the youth e-cigarette epidemic has been the availability of flavors in e-cigarette products.

Flavors in tobacco products are attractive to youth. Recent results from the 2019 National Youth Tobacco Survey show 72.2 percent of high school students that used e-cigarettes used flavored products. The most popular flavors were fruit (over 66%) and mint and menthol (57.3%).[9] Flavored tobacco products, including cigars, hookah and smokeless are also very attractive to youth. Overall, close to 70 percent of high school students who used tobacco products used a flavored product in the past 30 days in 2019.[10]

The American Lung Association and the American Thoracic Society do not believe that any flavored tobacco product should receive a PMTA authorization because flavors attract youth to use tobacco products. Any application that includes a flavor or flavor additive must demonstrate that it:

A. does not appeal to youth;
B. is substantially less harmful than smoking;
C. promotes cessation of all tobacco products or would not decrease total cessation of tobacco products;
D. would increase the number of smokers who completely stop using combustible products (users of this product are shown to switch completely) as a pathway to quitting the use of all tobacco products; and
E. provide detailed information on toxicity of such flavors and demonstrate that a flavored product is appropriate for the protection of public health.

In addition, however, it is important for FDA to use the PMTA process to ensure that the concept of "tobacco flavoring" is not misused. Before a PMTA for a tobacco-flavored product is issued, FDA should condition the PMTA on the use of a specified, precise formula for such flavoring to prevent manufacturers from changing the formulation of the flavor. In the absence of such a requirement, a manufacturer might seek to develop a range of "tobacco" flavors that could appeal to youth. [1]

It is also essential for FDA to condition the grant of any PMTA for a tobacco-flavored product on the requirement that a company not market the same product under a different name or label. In the absence of such a requirement, a company might use packaging, labeling, color or advertising and marketing code-words, such as "fresh," "tropic," "arctic," "cold," "bright," or "special" to suggest implied flavor characteristics and circumvent flavor restrictions.

[1] In addition, FDA must establish a product standard to remove all remaining flavored products from the marketplace, including flavored cigars and menthol cigarettes. In order to do this, FDA must create a product standard to define what constitutes a "tobacco" flavored ENDS

It has been a common practice in the marketing of cigarettes for a manufacturer to package a product with identical characteristics under different names in order to appeal to different segments of the market. The final PMTA rule should be designed to condition a marketing order on the marketing of a product under a single name and label. A manufacturer wishing to market such a product under a different name or label should be required to obtain a separate marketing order authorizing such marketing.

Beyond flavored e-cigarettes or Electronic Nicotine Delivery Systems (ENDS), FDA must also protect youth, adult nonusers and former users from other tobacco products seeking a PMTA – including cigars, smokeless, hookah and novel products. In light of the appeal of flavored tobacco products to young people, and the absence of any public health benefit from such products, there is no justification for the grant of a PMTA for any flavored product.

3. Abuse Liability

An essential contributor to the youth e-cigarette epidemic has been introduction of protonated nicotine (nicotine salts), which enables e-cigarette products to deliver a far more potent dose of nicotine to the user, with a resultant sharp increase in abuse liability. The comment of the other public health organizations deals with this issue in detail and the undersigned endorse those comments.

4. Evaluating Youth Risk Perception and Product Attractiveness to Youth

FDA must prioritize protecting those who do not use tobacco products by requiring affirmative documentation and compelling evidence demonstrating that the product will not be attractive to youth nor increase youth tobacco product use. This will require carefully and ethically designed youth perception studies that do not create youth interest in individual products. And while preventing youth initiation must be the priority, PMTA applications must require documentation and compelling evidence demonstrating that the product will also not increase initiation of tobacco product use by adults who do not use tobacco products. Further, FDA also must safeguard those that have successfully stopped using tobacco products from relapsing and re-initiating use with a product that receives a PMTA order.

Enforcement

No matter what requirements are put in place in the PMTA process, that process will be meaningful only if the provisions established by FDA are effectively enforced. Such enforcement will, at a minimum require all of the following:

- Products without complete and accepted applications by May 12, 2020 must actually be removed from the market, both online and brick-and-mortal retailers.
- Products for which PMTAs are not granted by May 12, 2021 and that are not granted extensions must actually be removed from the market by that date.
- Conditions contained in PMTA orders must be strictly adhered to.
- Post-market surveillance and reporting requirements must be strictly enforced.

Unfortunately, FDA's record of enforcement against new tobacco products that are being marketed illegally is woeful. Despite the fact that the introduction of new tobacco products or modification of a new tobacco product subsequent to August 8, 2016 has been illegal, many thousands of new products have been introduced and scores of them continue to be introduced virtually every day. Moreover, new products sold on August 8, 2016 have been continually modified in violation of law. For example, products on the market on August 8, 2016 have been modified to introduce nicotine salts and thereby vastly increase the potency of nicotine delivery. All these changes have come about without an effective response by FDA. FDA must do more than issue orders; it must enforce them promptly and effectively.

Other Important Features of PMTAs or the PMTA Process

1. <u>There should be no presumption about the relative harm of an ENDS product; each product must document that it is appropriate for the protection of public health.</u>

Each product application must submit full and complete information about the health risks of their product including all of its ingredients. The applications must include the toxicological profile, pharmacological profile, patterns of use, abuse liability, and use topography of the product. Information about the health risks of the products should consider the effects on both healthy individuals and sensitive subpopulations, such as people with lung disease.

Each individual PMTA application must provide data and analysis of the health impact of the specific product, as the public will actually use it. Therefore, FDA should prioritize evidence about real world actual use over clinical trials or laboratory studies. The application must show that the products are manufactured in ways that assure the FDA that the products perform in a consistent manner when actually used by consumers. FDA must require manufacturing data, including post-market information that will document how the product that receives a PMTA order performs in the real world. As noted above, the nicotine delivery from products that permit containers of liquids to be inserted into heating devices with varied levels of power cannot be determined and therefore no accurate evaluation can be made of their abuse potential. Applications for such products should not be granted.

The ongoing experience with E-cigarette, or Vaping Product Use Associated Lung Injury (EVALI) with well over 2, 409 cases in all 50 states and 52 deaths as of December 10, has shown that lack of information about the products that are available to consumers including ingredients, use patterns and abuse liability requires FDA to closely evaluate all tobacco products and devices that can be used to ingest nicotine along with other substances to determine if a device may receive a PMTA authorization.

2. <u>Promotes cessation of all tobacco products, including the PMTA product and does not decrease total cessation</u>

Switching from one tobacco product to another is not cessation. We know that 68 percent of cigarette smokers desire to quit[11] and we know that adult cigarette smoking prevalence is at an historic low of 13.7 percent.[12] No PMTA authorized product should undermine this public health progress. As such, the applications must show how a PMTA product's marketing will

not undermine adult smokers desire to quit and post market surveillance must show that the product does not undermine or reduce total tobacco cessation.

ENDS and other tobacco products that may receive a PMTA continue to pose significant health risks to users. As such, any PMTA that FDA grants must prioritize the complete cessation of the use of all tobacco products and as such no product in its marketing or as it is used by consumers must undercut cessation.

3. Dual and Poly Use

Many studies document that adult users of ENDS continue to use other tobacco products and dual and poly use of tobacco products is prevalent among youth. In 2017, the latest year that we have data for, 50 percent of adult e-cigarette users also currently smoked cigarettes.[13] In 2018, 41.7 percent of high school students who used tobacco products used two or more tobacco products.[14] All PMTA submissions must document whether current tobacco product users will start using the new PMTA tobacco product as a pathway to quitting all tobacco product use, including the PMTA product. Switching to a new product is not quitting and users of all PMTA products experience health risks.

Applications must show whether the product will be used exclusively, or if users will continue to use other products including traditional cigarettes or other combustible products. Applicants must show that their product puts users on a pathway to quitting the use of all tobacco products. FDA must consider the public health impacts on the population, and dual use as well as whether a product puts users on a pathway to quitting use of all tobacco products as explicit factors FDA must consider before issuing a PMTA marketing order. Post-market surveillance must show who is using a PMTA product and what other products are also being used or if these products are being used exclusively.

A new longitudinal study published on December 16, 2019 in the *Journal of Preventive Medicine* found that e-cigarette use significantly increases a person's risk of developing chronic lung diseases like asthma, bronchitis, emphysema or chronic obstructive pulmonary disease. The study also found that dual users, people who used e-cigarettes and also smoked tobacco, were at an even higher risk of developing chronic lung disease than those who used either product alone.[15] PMTA must account for the health risks posed by dual use.

In addition, products on the market should be required to include surveillance and information from their time on the market. Post-market surveillance also must document product users to quit using all tobacco products.

4. All PMTA applications must be complete

FDA should promptly reject incomplete applications. FDA delineated all of the information required for an application including the format that the information is to be submitted. If an incomplete or invalid application is submitted, FDA must reject that application and issue an order directing the product to be removed from the market no later than May 12, 2020 or the date of the FDA's determination to reject the application. Similarly, if FDA determines during

the review of an accepted application that said application is incomplete or invalid, FDA must issue an order directing the product to be removed from the market on May 12, 2020 or the date of the FDA order.

The American Lung Association and the American Thoracic Society oppose the proposed supplemental PMTA or a resubmission. FDA should only consider complete applications. FDA must not allow "modified versions" of a product that had received a PMTA to circumvent the clear statutory requirements that products that are not substantially equivalent to products on the market prior to February 15, 2007 must go through the PMTA review.

5. Transparency and Public Participation

The proposed rule creates a PMTA process that excludes public participation and undermines enforcement and protection of the public health. At minimum, FDA should publicly disclose each PMTA upon receipt and then publicly disclose if a PMTA submission is accepted for review or rejected. FDA should also open a docket for each PMTA that allows all stakeholders to submit information to inform FDA's review. Unlike other FDA product reviews, many of these tobacco products have been on the market for years. The result is a trove of independent research and data on the use and abuse of the products. In order for FDA to determine whether an application is appropriate for the protection of public health, FDA should be fully informed of all relevant information. Further, after May 12, 2020, if a product is on the market but has not submitted a complete application that FDA has accepted for review, the public has a right to know that these products are not compliant and subject to enforcement action. The public must be able to report such products to the FDA for appropriate action.

Finally, we strongly oppose FDA permitting the redaction of the marketing plans from PMTA marketing orders as was done with the recent IQOS order. These marketing plans must be publicly disclosed to ensure that the PMTA order is consistent with the law and the product will not be marketed to nonusers especially children and will not result in a reduction of the number of people who quit smoking.

Criteria for Granting a PMTA

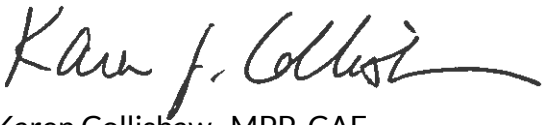
For the reasons stated above, FDA should not grant a PMTA in the absence of scientific evidence that demonstrates that the marketing of the product has not and will not appeal not appeal to youth; is substantially less harmful than smoking; promotes cessation of all tobacco products or would not decrease total cessation of tobacco products; and would increase the number of smokers who completely stop using combustible products (users of this product are shown to switch completely) as a pathway to quitting the use of all tobacco products.

The final PMTA rule adopted by FDA must require manufacturers to produce sufficient scientific information to enable FDA to determine whether these criteria have been met.

Thank you for the opportunity to provide these comments.

Sincerely,

Harold P. Wimmer
National President & CEO
American Lung Association



Karen Collishaw, MPP, CAE
Chief Executive Officer
American Thoracic Society

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