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Dockets Management Staff (HFA-305)
U.S. Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2018-N-3504

The Campaign for Tobacco-Free Kids (Tobacco-Free Kids) submits these comments in connection with the public meeting convened by the U.S. Food and Drug Administration (FDA) on Tobacco Product Application Review on October 22-23, 2018. These comments supplement, and incorporate by reference, the comments made at the hearing by the undersigned, on behalf of Tobacco-Free Kids.

FDA Must Ensure that New Tobacco Products Are Subject to Premarket Review

The current epidemic of youth usage of JUUL and other e-cigarette products is a powerful demonstration of what can happen when new tobacco products are allowed to reach the market without undergoing the premarket review required by the Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act or TCA). Indeed, there is little doubt that FDA's delay in issuing a deeming rule regulating e-cigarettes and other tobacco products, and its subsequent suspension until 2022 of premarket review of new e-cigarettes on the market when the deeming rule became effective, have allowed companies like JUUL Labs to irresponsibly market new products that are extraordinarily appealing to young people. Indeed, there is little doubt that had FDA not delayed issuing a deeming rule regulating e-cigarettes and other tobacco products until 2016, and had FDA not suspended until 2022 the requirement that e-cigarette manufacturers submit their applications for premarket review, some of the products, and many of the practices engaged in by irresponsible companies like JUUL Labs, in marketing new products that are extraordinarily appealing to young people, might have been prevented or not even tried.

FDA deserves credit for recognizing that there is now an epidemic of e-cigarette use by young people attracted to highly flavored products that have been marketed with images and in forums that appeal to young people. FDA also deserves credit for beginning to take some steps to rein in where some of these products are sold and how these products are being marketed. However, the steps FDA recently announced to address the epidemic of youth e-cigarette use are likely to be inadequate to the task. The agency will always be playing catch-up because it continues to allow the sale of these products without premarket review of the full range of their implications for individual and public health.

Moreover, as we have emphasized in prior correspondence with FDA, e-cigarette companies have continued to introduce new products without marketing orders after the August 8, 2016 effective date of the deeming rule. FDA has sent requests for information to 21 companies that appear to have illegally marketed their products without marketing orders, but it is unclear what follow-up action has

been taken. We urge the agency to require all companies with newly-deemed products on the market to submit evidence that they were on the market as of August 8, 2016 and thus are covered by FDA's current compliance policy.

FDA Should Make It Clear that the Purpose of Premarket Review Is to Enhance Public Health, Not to Allow the Introduction of Products that Do Not Do So

The testimony by various industry representatives during the meeting revealed a basic misunderstanding of the governing objective of the premarket review process. Implicit in the various industry comments was the idea that FDA's statutory authority over these products was intended to assure companies a speedy, easy pathway to market for new tobacco products without regard for their impact on the public's health. As FDA itself has recognized, this approach is entirely inconsistent with the public health standard by which new products are to be measured. Rather, the statutory standard requires a showing that a new product actually enhances the public health before a product can be marketed.

For new tobacco products that are not "substantially equivalent" to a grandfathered product, the manufacturer has the burden of showing that the marketing of the product is "appropriate for the protection of public health." In granting the first PMTA to Swedish Match for its Swedish snus products, FDA interpreted this standard to require demonstration of a positive public health benefit from introduction of the new product:

> One of FDA's goals is to decrease morbidity and mortality from tobacco use and *to change the status quo* so that nearly half a million Americans no longer die every year from tobacco use. Therefore, the broad overall objective of authorizing new tobacco products to be marketed through the PMTA process is to *reduce the morbidity and mortality from tobacco use*. [1]

Similarly, in its responses to "Commonly Asked Questions" about premarket review on its website, FDA states that PMTAs must provide scientific data "to demonstrate that the new tobacco product is beneficial to the population as a whole including users and non-users." In its communications with industry about the standard governing the introduction of new tobacco products, FDA should make it clear that the objective of FDA review is to ensure that new products actually benefit public health, not to simply maintain the status quo and not to ensure industry an easy pathway to market.

Previously-issued FDA Guidances Are Sufficient to Allow Manufacturers of Deemed Products to Submit Premarket Tobacco Product Applications

FDA's two-day meeting on premarket tobacco product applications gave the agency an opportunity to restate the clear, objective conditions that a manufacturer needs to address in their preparation of applications for a marketing order. Although the companies complained that FDA had not issued clear foundational documents, FDA's presentations at the October hearing made clear that those allegations have no merit. Indeed, even as FDA moves forward, it should be recognized that FDA

[1] FDA, Premarket Tobacco Application (PMTA) Technical Project Lead (TPL) Review for Swedish Match of North America, Inc. (Nov. 3, 2015), at 34 (emphasis added).

is not writing on a blank slate. On the contrary, FDA has previously issued detailed Draft Guidances on each of the topics covered at the public hearing that provide clear criteria and guidelines.[2]

FDA issued its first guidance on PMTA applications in September, 2011, over seven years ago. *See* FDA, *Guidance for Industry: Applications for Premarket Review of New Tobacco Products* (Sept. 2011). Moreover, when FDA issued the deeming rule, it issued another guidance document on the same topic, focused on e-cigarettes. *See Draft Guidance for Industry: Premarket Tobacco Applications for Electronic Nicotine Delivery Systems* (May 2016). Although FDA has suspended the requirement of premarket review of newly-deemed product for years to come, repeatedly citing the need for time to issue regulations on what information is expected from companies in premarket applications and to give manufacturers more time to submit quality applications, the two-day meeting failed to identify any deficiencies in these previous Guidances that would leave companies unable to file quality applications right now.

A month before the meeting, Commissioner Gottlieb made it clear that there is "no excuse for manufacturers not to file applications with the FDA because the agency hasn't told them what they are expected to do."[3] There also is no excuse for FDA to suspend premarket review until 2021 for cigars and until 2022 for e-cigarettes because companies lack sufficient information to allow them to submit PMTAs. Indeed, in his November 15 Statement, Commissioner Gottlieb expressed hope that he would "soon see manufacturers of ENDS products preparing, with the FDA input as appropriate, premarket tobacco product applications (PMTAs) to demonstrate that their products meet the public health standard in the Tobacco Control Act."[4] This statement recognizes the central role that the premarket review process should play in ensuring that ENDS products, as they are actually used, provide benefits to public health that outweigh their costs and that FDA has already provided sufficient guidance to manufacturers of these products to permit them to file premarket applications.

New Tobacco Products Must be Reviewed Individually Because Different Product Characteristics Can Have Significant Public Health Consequences

While the industry complains about the burden of providing information about individual products for purposes of premarket review, it is essential for FDA to evaluate products individually because different product characteristics impact toxicity, likelihood of dual use and/or cessation, abuse liability and attractiveness to non-smoking youth. While it may or may not be possible for FDA to develop standards to more broadly address many of these issues, at present FDA must require manufacturers to provide the information needed to make these assessments for individual products. If anything, it will be difficult to develop appropriate standards for categories of products without product information acquired from individualized review. The responsibility to provide relevant information

[2] On substantial equivalence reports, FDA has issued the following guidances: *Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products* (January 2011); *Draft Guidance for comments – Substantial Equivalence Reports: Manufacturer Requests for Extensions or to Change the Predicate Product* (July 2014); *Demonstrating the Substantial Equivalence of a New Tobacco Product: Responses to Frequently Asked Questions* (Dec. 2016, 3rd ed.) (previous editions published March 2015 and September 2015). On modified risk applications, FDA has issued a *Draft Guidance for Industry – Modified Risk Tobacco Applications* (March 2012).

[3] Statement from FDA Commissioner Scott Gottlieb, M.D., on new steps to address epidemic of youth e-cigarette use (Sept. 12, 2018).

[4] Statement from FDA Commissioner Scott Gottlieb, M.D., on proposed new steps to protect youth by preventing access to flavored tobacco products and banning menthol in cigarettes (Nov. 15, 2018) at 5.

about individual products is routinely accepted by manufacturers of other products under FDA's drug and device jurisdiction.

What we are learning about e-cigarettes underscores the need for attention to individual product differences, given the multitude of examples in the published literature showing that the toxicity of different flavorings or other constituents of an e-cigarette vary depending on the temperature of the heating device, its efficiency, how a consumer uses the product in the real world and other factors. Certainly the emergence of JUUL, with product characteristics and population-wide consequences totally unlike the e-cigarette products that preceded it, shows the public health importance of highly individualized product review.

Product Review Must Consider Multiple Factors Beyond the Characteristics of the Product Itself

As FDA has acknowledged in its previously published Guidances, and reiterated in its November 15, 2018 announcement, while it is necessary for companies to provide information about the product itself in the premarket review process, companies must also provide information to enable FDA to evaluate how, and by whom, the product will be used. This necessarily entails the assessment of information about how the product will be marketed. The current epidemic of youth e-cigarette addiction resulting from JUUL and similar products is a powerful object lesson about the critical importance of comprehensive premarket review, including review of marketing materials. If FDA had acted sooner to subject e-cigarettes to regulation, and thus to premarket review, the agency would have been in a far better position to address the sophisticated and youth-targeted social media marketing that contributed to JUUL's appeal to underage users, as well as other features of the product that created a risk of initiation by young people. If FDA had followed the requirements of the Tobacco Control Act, it could have addressed this risk before these products caused a public health crisis.

FDA's Draft Guidance for PMTAs for ENDS products properly requires submission of evidence on a range of potential outcomes depending on the likely use of the product, including:

- The likelihood of current nonusers of tobacco products initiating or reinitiating tobacco use by using the new product;
- The likelihood that consumers will adopt the new product and then switch to other products that may present higher levels of risk, such as cigarettes;
- The likelihood of consumers using the new product in conjunction with other tobacco products;
- The likelihood of consumers switching to the product instead of ceasing tobacco product use or using an FDA-approved cessation product;
- Assessment of abuse liability; and
- Assessment of user topography.

Applicants for Premarket Orders Should Be Required to Submit Scientific Evidence on Consumer Perception by Youth of Products, Claims, Advertising and Labeling

The current epidemic of e-cigarette use by adolescents underscores the critical importance of requiring applicants to submit scientific information to allow FDA to assess the likelihood of initiation of product use by young people. Yet tobacco companies have not developed or submitted such evidence,

erroneously relying on statements by FDA that it is not required. For example, PMI's MRTP application for its iQOS heated tobacco product explained the absence of youth data with the statement that "PMI's internal policy prohibits the conducting of studies relating to tobacco products, which involves under legal age of smoking, a policy that is consistent with recommendations from the FDA."[5]

However, it is clear from FDA's Guidances that the agency believes data on youth perception to be important and is willing to work with companies to design studies that yield relevant information within appropriate ethical guidelines to ensure that the studies themselves do not create interest in tobacco products by youth – a statement FDA staff repeated at the October hearing. Thus, in its Draft Guidance for PMTAs for ENDS, FDA cites the importance of evaluations of the likelihood of initiation among never-users and former users of tobacco products, including "*scientific information on the likelihood of product use by youth*, young adults, pregnant women and other vulnerable populations."[6] (emphasis added.) Moreover, as the FDA Draft Guidance for the preparation of MRTP applications makes clear, FDA requires only that "all study subjects *receiving tobacco products* are current daily tobacco product users at least 21 years of age."[7] Not only is this limitation not applicable to studies of promotional material such as modified risk claims to determine the effect of such materials on adolescent risk perception or interest in using the product, but the FDA Guidance states that inclusion of the effect on adolescent perception should be an essential features of such studies. The Guidance states:

> To address the effect of the MRTP on tobacco use initiation, FDA recommends that applicants submit:
>
> - Human studies that evaluate consumer perception of the product, including its labeling, marketing and advertising.
>
> These studies should be designed to provide evidence regarding the likelihood of population benefit or harm from the proposed product, including . . . .:
>
> - The likelihood that consumers who have never used tobacco products, *particularly youth and young adults*, will initiate use of the tobacco product;[8]

Contrary to the false industry assertion that FDA has a policy that precludes research on consumer perceptions involving youth, as FDA staff repeated at the October hearing, FDA's guidance on MRTP applications offered applicants the opportunity to work with the agency to determine the best way to conduct studies involving youth.[9] FDA's approach is entirely consistent with the recommendations made by the Institute of Medicine's (IOM) 2012 report, *Scientific Standards for Studies on Modified Risk Tobacco*, which stated that "FDA should require studies to include populations of special relevance, including (but are not limited to). . . Adolescents"[10] and included an assessment of the effects on youth as "an essential element in establishing the public health benefit of an MRTP."[11] The IOM Report

[5] PMI Modified Risk Tobacco Application for iQOS, Sec. 2.7, at 126.
[6] FDA Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems Guidance for Industry, Draft Guidance (May 2016), at 36 (emphasis added).
[7] FDA Draft Guidance, Modified Risk Tobacco Applications (March 2012), at 29 (emphasis added).
[8] *Id.* at 20 (emphasis added).
[9] *Id.* at 26.
[10] IOM Report at 14.
[11] *Id.* at 50.

detailed ideas for how research on youth perceptions of risk of MRTPs can be conducted consistent with ethical standards.[12]

Thus, given the industry's insistence that FDA policy precludes research into youth perception as part of the premarket review process, FDA needs to make it clear going forward that no such policy exists, that the agency is prepared to work with applicants to design studies that are consistent with ethical standards, and that an applicant's failure to present youth perception evidence may be a sufficient reason for denial of a PMTA or a MRTP application.

The PMTA Process Should be Made More Transparent and Should Accommodate Public Comment

Although the Tobacco Control Act requires that MRTP applications be made available for public comment, it imposes no such requirement for PMTAs. Yet an FDA decision to grant a PMTA could be just as consequential for public health as the grant of a MRTP application. It is certainly within FDA's authority to facilitate greater transparency and public participation in the PMTA process, even though the statute does not require it. Companies could be allowed to redact sensitive commercial material, as they are in MRTP applications, yet FDA would be given the benefit of public input on the likely impact of the new tobacco product on public health. We therefore urge FDA to make the PMTA process more transparent and amenable to public participation.

Respectfully submitted,

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[12] *Id.* at 10.