February 5, 2018

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

Re: Comments in Docket No. FDA-2017-N-5101, Review of Existing Center for Drug Evaluation and Research Regulatory and Information Collection Requirements

The undersigned organizations submit these comments in the above-designated docket to urge the Center for Drug Evaluation and Research (CDER) to re-evaluate its critical role in reducing tobacco-related disease and death and adopt policies that actually increase the availability and use of safe and effective smoking cessation therapies.

The stated purpose of FDA's solicitation of comments in this docket is to receive public input on "ways we can change our regulations to achieve meaningful burden reduction while continuing to achieve our public health mission and fulfill statutory obligations." 82 Fed. Reg. 42499 (September 8, 2017). To fulfill this objective, FDA should critically examine CDER's regulation of nicotine replacement therapy (NRT) and other smoking cessation products and institute policies that would create a regulatory environment that encourages the development of innovative therapies that will increase the number of smokers who use these therapies without increasing the risk of addicting non-smokers. FDA's current policies have not achieved this objective.

In July of this year, when Commissioner Gottlieb set out his new "comprehensive approach to nicotine and tobacco," he described it as "an FDA-wide imperative," that "means we must also work to have medicinal nicotine and other therapeutic products play a greater role in helping more smokers try to quit with help, to quit successfully, and to stay quit." He then specifically directed CDER "to examine possible steps we can take to address the performance of medicinal nicotine products, including the speed with which the nicotine is delivered, and other possible innovations in treatments that could help more smokers use FDA-approved products to quit smoking." Any CDER review of existing regulatory policy must place the highest priority on responding to Dr. Gottlieb's direction. FDA's recent creation of a new Nicotine Steering Committee, consisting of senior leadership from CDER, the Center for Tobacco Products (CTP)

and the Office of the Commissioner,[1] and its convening of the January 26 public hearing on FDA's approach to evaluating NRT products,[2] represent concrete steps in the right direction.

In its notice soliciting comments in this docket, FDA states that it "promotes the public health by fostering and supporting innovative approaches and solutions for some of our nation's most compelling health and medical challenges." 82 Fed. Reg. at 42500. There is certainly no more compelling health challenge facing our nation than the disease and death from smoking. Cigarette smoking causes more than 480,000 premature deaths every year – the leading preventable cause of death in the United States, taking more lives annually than AIDS, alcohol, car accidents, illegal drugs, murders and suicides combined. Although great progress has been made in reducing smoking rates over several decades, over 36 million Americans are current smokers. Half of them will likely die prematurely from smoking-related disease. They are in urgent need of innovative new therapies that will help them quit.

In the last 50 years, the FDA has approved only three drugs (NRTs, bupropion and varenicline) as safe and effective in smoking cessation. It has approved no new medications in the last decade and it places restrictions on existing products and the use of those products that curtail their reach and efficacy. Although almost 70% of smokers want to stop smoking and more than half tried to stop within the past year, fewer than one-third who tried to stop used any FDA-approved medications and only about 7% of smokers actually stopped smoking successfully in the past year.[3]

In calling for a reexamination of the need for new and innovative smoking cessation products, Dr. Gottlieb was echoing a similar directive from the United States Congress when it enacted the Family Smoking Prevention and Tobacco Control Act of 2009 (TCA). In Section 918 of the Food, Drug & Cosmetic Act, as amended by the TCA, Congress directed FDA to issue a report, within three years,[4] examining "how best to regulate, promote and encourage the development of innovative products and treatments . . . to better achieve" three objectives: (1) total abstinence from tobacco use; (2) reductions in consumption of tobacco; and (3) reductions in the harm associated with continued tobacco use. Section 918 also directed FDA to consider several approaches to expedite approval of new safe and effective tobacco cessation products and to facilitate more effective use of existing approved products, including considering the designation of smoking cessation products as fast track products to benefit from expedited

[1] Scott Gottlieb, Janet Woodcock and Mitchell Zeller, "Advancing Medicinal Nicotine Replacement Therapies as New Drug – a new step in FDA's comprehensive approach to tobacco and nicotine," FDA Voice (Nov. 29, 2017).
[2] *See* 82 Fed. Reg. 56759 (Nov. 30, 2017).
[3] Babb, Stephen, et al., "Quitting Smoking Among Adults, United States 2000-2015," MMWR 65(52) 1457-1464, 2017.
[4] *See generally,* Dept. of Health and Human Services, Food and Drug Administration, "Report to Congress: Innovative Products and Treatments to Achieve Abstinence from Tobacco Use, Reductions in Consumption of Tobacco, and Reductions in the Harm Associated with Continued Tobacco Use, Required by Section 918 of the Federal Food, Drug, and Cosmetic Act, as Amended by Public Law 111-31."

approval, considering the approval of extended use of nicotine replacement therapies (NRTs) for the treatment of tobacco dependence, and considering additional indications for NRTs, such as for craving relief or prevention of relapse. Although FDA issued its report to Congress in 2013, the agency has only supported some modest changes to the labeling of NRTs and has yet to chart a path toward more effective cessation treatments. Much more needs to be done.

FDA should engage in a searching review of FDA's approach to nicotine-containing products, which should be carefully coordinated between CDER and the Center for Tobacco Products, with the following objectives[5]:

(1) Ensuring that the evaluation of possible new indications or labeling changes for existing approved smoking cessation products are based on a risk/benefit analysis that uses, as the relevant comparator, that the failure to use these products results in the continued use of a product that kills half of its long-term users;
(2) Determining whether indications and labeling for existing approved smoking cessation products need to be revised to encourage greater consumer acceptance and more effective use of those products;[6]
(3) Evaluating how FDA's current approaches should be revised to encourage greater innovation in the development and availability of new smoking cessation products;
(4) As suggested by Dr. Gottlieb in his July remarks, examining the speed with which nicotine is delivered by these products as a factor in evaluating their effectiveness as cessation tools;
(5) Implementing procedures for fast track, other accelerated approval authorities and post-market surveillance that can facilitate approval of new and effective treatments for tobacco dependence; and
(6) Establishing a division of responsibilities between CDER and CTP that best promotes innovation in the development of products that benefit public health.

Finally, the dramatic changes in the market for nicotine products that have occurred since FDA issued its Report to Congress under Section 918 add urgency to the need for a reassessment of the agency's approach to medicinal nicotine products, as well as the need for close

[5] *See generally*, Comments of Campaign for Tobacco-Free Kids in Docket No. FDA-2016, Psychopharmacologic Drug Advisory Committee and Drug Safety and Risk Management Advisory Committee meeting of September 14, 2016 (August 30, 2016).

[6] In response to various Citizen Petitions, in 2013 FDA determined that certain statements in FDA-approved labels of over-the-counter nicotine replacement therapy products, related to concomitant use with other nicotine-containing products and duration of use, can be modified. *See* FDA, "Modifications to Labeling of Nicotine Replacement Therapy Product for Over-the Counter Human Use," 78 Fed. Reg. 19718 (April 2, 2013). However, researchers have found that, despite these label changes, FDA should include "more explicit statements regarding the different conditions in which NRT is safe and effective, in line with current research evidence." L.M. Lucito, et al., "Addressing the Evidence for FDA Nicotine Replacement Therapy Label Changes: A Policy Statement of the Association for the Treatment of Tobacco Use and Dependence and the Society for Research on Nicotine and Tobacco," *Nicotine & Tobacco Research*, Vol. 16, No. 7 (July 2014), at 909-914. *See also* C. Winchell, et al., "Letter: Food and Drug Administration Response to the ATTUD/SRNT Policy Statement on the Labeling of Nicotine Replacement Therapies," *Nicotine & Tobacco Research Advance Access*, July 6, 2015.

coordination between CDER and CTP to make that reassessment part of a comprehensive agency-wide nicotine regulatory policy. The e-cigarette experience provides a compelling example. The ruling in *Sottera, Inc. v. FDA*, 627 F.3d 891 (D.C. Cir. 2010) that e-cigarettes cannot be regulated by FDA as drugs or devices absent therapeutic claims, but could be regulated as "tobacco products" under the TCA, along with FDA's lengthy delay in asserting its jurisdiction over e-cigarettes by issuing a final rule deeming them subject to its jurisdiction as "tobacco products" under the TCA, allowed the emergence of a substantial unregulated market for highly addictive e-cigarettes and their widespread use by youth and young adults. By virtue of FDA's inaction on both the CTP and CDER side, we now face a market reality that a whole new class of addictive nicotine products is readily available to the general public for recreational and other uses, and e-cigarettes, sold with a dizzying array of flavors that make them appealing to young people, have become the most popular tobacco product among high schoolers. Moreover, the recent report of the National Academies of Sciences, Engineering and Medicine, *Public Health Consequences of E-Cigarettes* (NASEM Report), found that, "for youth and young adults, there is substantial evidence that e-cigarette use increases the risk of ever using combustible tobacco cigarettes."[7]

Millions of smokers are looking for alternative nicotine-delivery products to help them stop smoking. Because of FDA's lack of action at both CDER and CTP, some of those smokers use e-cigarettes instead of using FDA-approved medicinal products, even without any FDA pre-market review of products to determine whether any particular e-cigarette product actually helps people switch and stop smoking combustible tobacco. FDA's failure to create a regulatory environment that encourages the development of more effective medicinal products, combined with the un-regulated e-cigarette market, have led to significant public health problems.

Now that FDA has jurisdiction over the full range of products containing nicotine derived from tobacco, it must use that authority to design a comprehensive policy that both protects the public from the risks posed by inadequately regulated tobacco products and creates a regulatory structure that will meet the urgent need for more effective therapeutic products. No agency-wide approach to nicotine regulation can sufficiently protect public health without CDER exercising its full range of regulatory options to foster innovation and help more smokers use FDA-approved products to quit smoking.

Respectfully submitted,
Campaign for Tobacco-Free Kids
Tobacco Control Legal Consortium
Truth Initiative

[7] National Academies of Science, Engineering and Medicine, *Public Health Consequences of E-Cigarettes*, Consensus Study Report Highlights (January 2018).