1400 EYE STREET, N.W. • SUITE 1200 • WASHINGTON, DC 20005
PHONE (202) 296-5469 • FAX (202) 296-5427

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Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852
Re: Docket No. FDA–2012–N–1148

The Campaign for Tobacco-Free Kids hereby submits comments in the above-designated docket in response to FDA's request for comments related to Actions Related to Nicotine Replacement Therapies and Smoking-Cessation Products; Report to Congress on Innovative Products and Treatments for Tobacco Dependence.

Despite declines in smoking over the last several decades, tobacco use remains the leading preventable cause of death in the United States, with more than 430,000 Americans dying an early death from tobacco use every year.[1] While the only way to completely avoid the risks of smoking is to never start, substantial benefits accrue from quitting no matter how long you have smoked.[2]

[1] Centers for Disease Control and Prevention (CDC), "Smoking-Attributable Mortality, Years of Potential Life Lost, and Productivity Losses—United States, 2000–2004," *Morbidity and Mortality Weekly (MMWR)* 57(45), November 14, 2008, http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5745a3.htm. See also, U.S. Department of Health and Human Services (HHS), *How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-Attributable Disease: A Report of the Surgeon General.* Atlanta, GA: U.S. Department of Health and Human Services, CDC, 2010.

[2] HHS, *The Health Benefits of Smoking Cessation: A Report of the Surgeon General.* Atlanta, GA: U.S. Department of Health and Human Services, CDC, 1990. See also, HHS, *How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-Attributable Disease: A Report of the Surgeon General*, Atlanta, GA: U.S. Department of Health and Human Services, CDC, 2010. HHS, *The Health Consequences of Smoking: A Report of the Surgeon General*, Atlanta, GA: U.S. Department of Health and Human Services, CDC, 2004.

Despite the known risks of smoking and the benefits of quitting, far too few smokers quit successfully. While 70 percent of smokers say they want to quit and half of all smokers report a quit attempt in a given year, only four to seven percent of those who try during the course of a year succeed.[3] While this is largely attributable to the addictive power of nicotine and efforts by the tobacco companies to keep people smoking, the fact that most smokers do not more often utilize evidence-based interventions—counseling and medication—in their quit attempts also contributes greatly to the low rate of success. [4] However, even those who do get help in quitting are more likely to fail than to succeed in their attempt. While the evidence is clear that smoking cessation medications work when used appropriately, even the best quit rates, at 19-33%, are less than optimal. [5]

It is clear that we need to make better use of existing interventions and find more and better ways to help smokers quit. The FDA is in a position to make that happen. With the passage of the Family Smoking Prevention and Tobacco Control Act (FSPTCA), the FDA—through the Center for Tobacco Products (CTP) and the Center for Drug Evaluation and Research (CEDR)—now has the authority to regulate tobacco and all other nicotine products in all their forms: cigarettes, smokeless, gum, patch, inhaler, cigars, e-cigarettes, toothpicks, or whatever form is developed.

This gives FDA the opportunity to address both the addictive nature of tobacco products AND the availability and efficacy of products that help smoker quit. FDA must use this authority and coordinate across Centers to establish a regulatory scheme that will both maximize FDA's power to reduce the use of tobacco products that addict and kill AND increase the availability, effectiveness and use of products that can help people quit using tobacco products that cause death and disease. FDA's responsibility is to promote the public health. There is little that FDA

[3] Fiore, MC, et al, *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline*, Rockville, MD: U.S. Department of Health and Human Services, May 2008. See also, CDC, "Quitting Smoking Among Adults—United States, 2001–2010," *MMWR* 60(44), November 11, 2011, http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6044a2.htm?s_cid=%20mm6044a2.htm_w.

[4] Fiore, MC, et al, *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline*, Rockville, MD: U.S. Department of Health and Human Services, May 2008. See also, CDC, "Quitting Smoking Among Adults—United States, 2001–2010," *MMWR* 60(44), November 11, 2011. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6044a2.htm?s_cid=%20mm6044a2.htm_w.

[5] Fiore, MC, et al, *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline*, Rockville, MD: U.S. Department of Health and Human Services, May 2008.

can do to save more people from premature death than to aggressively and creatively use these complementary authorities.

The rapid and ongoing expansion of novel nicotine delivery products and recent court decisions about how they should be regulated make it more urgent that FDA first act quickly to assert jurisdiction over these products and then develop a comprehensive approach to regulating all nicotine based products—whether overseen by CTP or CEDR—in a manner that is designed to minimize the death and disease caused by current tobacco products. The decision in Sottera, Inc. v. FDA, 627 F.3d 891 (D.C. Cir. 2010) directed that products that contain no tobacco but do contain nicotine derived from tobacco (e.g. e-cigarettes, some nicotine lozenges) be regulated by CTP rather than CEDR—unless a therapeutic claim is made for the product. This has created a gaping loophole that needs to be closed quickly by the assertion of jurisdiction by FDA over these products. It also means that some products that are virtually the same will be regulated by different Centers based on the claims made about the products. This will include CTP's authority under Sec. 911 of the FSPTCA over any claims of modified risk as well as CEDR's authority over claims that cross the line to therapeutic claims and claims related to smoking cessation. It is, therefore, essential that the Centers work in coordinated fashion to regulate the huge variety of tobacco and nicotine products on the market and the ways they are marketed.

By coordinating across Centers, the FDA can develop a comprehensive approach that makes it easier for smokers to quit and provides more and better ways to help them do so. This approach includes the following:

By CTP:

- Reducing the addictive power of tobacco products and the ability of the tobacco industry to appeal to and attract children; and
- Carefully limiting modified risk claims so that they do not discourage smokers from quitting.

By CEDR:

- Making existing evidence-based cessation medications more available, more attractive, and more effective for smokers;
- Fostering innovation in bringing new cessation products to the market; and
- Without weakening the current scientific safety safeguards, adopting an approach that weighs the risk of cessation products against the risk of continued smoking and the more than 430,000 Americans who die each year from tobacco use.

Reducing the Addictive Power of Tobacco Products

On the tobacco side, CTP should fund and foster research on the best way to reduce or eliminate the addictive nature of tobacco products, as well as the ways the tobacco industry makes tobacco products attractive and appealing to non-smokers, especially children. The tobacco industry has a long history of actions to ensure that smokers get the optimum dose of nicotine to get and keep them addicted. Therefore, understanding this and the ways to minimize addiction are critical. It should also carefully examine the myriad ways that the tobacco companies have used ingredients and design characteristics to make tobacco products appealing to children. CTP has the authority to then take strong regulatory action, including product standards, based on that science. This approach should take into account not only potential reductions in nicotine beyond levels that are addictive but also the ways tobacco companies make their products more addictive (e.g., use of ammonia). CTP must also make sure that the implementation of its authority over modified risk claims does not discourage smokers from quitting, as occurred with low-tar marketing. Modified risk claims must only be allowed when the public health benefit is clear and substantial and does not divert smokers from cessation products approved by CEDR.

Now that FDA has authority over all nicotine-based products, serious consideration should be given by CTP to adopting a principle that its actions should, to the extent possible and compatible with its statutory mandate, create an environment, incentives, and regulations that drive smokers away from products that addict and cause disease and toward nicotine-based products that do not cause disease. It should also be careful not to adopt policies that promote or encourage dual use—that is, use of disease causing tobacco products and other nicotine-based products—except, if the science warrants, as a path to total cessation.

The FDA should also be leery of product claims that are promoted to reduce the number of cigarettes smoked, unless as part of a scientifically validated method to reduce to quit. The public health benefits of reducing the number of cigarettes smoked are modest in contrast to the public health damage caused by longer-term smoking.

Developing New Approaches to Cessation

FDA must also move immediately to improve smoking cessation outcomes. Even as we work to make sure that all of the current evidence-based smoking cessation therapies are available and that their more effective use is encouraged for all tobacco users, we must develop new interventions that more smokers will use and that will help more of them quit.

Congress clearly recognized this in the FSPTCA in its Sec. 918 instruction to FDA to look at ways to:

- Generate greater consumer acceptance and use of existing smoking cessation products, and
- Foster innovation of new smoking cessation products that are more effective than products currently on the market.

To do this, FDA should work with industry to encourage innovation in a) examining how current NRT products can be used to increase the number of people who use those products and to increase the percentage of users who succeed in quitting, including changes in labeling and indication; and b) the development of new products that will be more effective in helping tobacco users quit.

A few key considerations are relevant to new indications for existing products, as well as the development of new products:

- It is critical that FDA compare the risks and benefits of these interventions to the undeniable risk, disease and death from continued smoking, rather than assume that there is no health harm from doing nothing new. With more than 430,000 Americans dying

from smoking every day, any risks of smoking cessation interventions must be weighed against this.

- FDA must preserve the safety and efficacy standard, even as it examines new indications and new products. Should the FDA consider surrogate markers for smoking cessation, such as reduced smoking, there must be clear evidence of a clear and substantial public health benefit, as well as evidence that the surrogate marker is predictive of smoking cessation. The benefits of reduced smoking that does not lead to cessation are modest and outweighed by the danger of prolonged smoking. The U.S. Surgeon General, among others, has concluded that "the strongest determinant of risk for many diseases (e.g., lung cancer) caused by tobacco use is the duration of smoking."[6]

- While encouraging innovation and wider availability of NRT, FDA must ensure that this does not simply serve to keep smokers smoking by serving as a bridge product that provides nicotine in times and in places where smokers cannot smoke, or by convincing them they are taking a step toward quitting when they are not. Again, anything that serves to keep smokers smoking longer will have a deleterious impact on public health.

With those considerations and caveats in mind, we support FDA working with industry to determine if indications and labeling for NRT products can be expanded or changed to improve cessation outcomes. A number of possible indications have been suggested and studied, and we encourage FDA to work with manufacturers to develop a process for more quickly determining if these approaches are warranted by the science. These approaches include:

- <u>Combination Therapies</u>. The Public Health Service Clinical Practice Guideline for smoking cessation recommends the use of combination therapies,[7] yet the

[6]U.S. Department of Health and Human Services. *How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-Attributable Disease: A Report of the Surgeon General.* Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2010. See also, *Cancer Research*, 63:6556, October 1, 2003.

[7]Fiore, MC, et al, *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline*, Rockville, MD: U.S. Department of Health and Human Services, May 2008. See also, CDC, "Quitting Smoking Among Adults—United States, 2001–2010," *MMWR* 60(44), November 11, 2011.

labeling for NRTs discourages such use. Revision of this labeling is an area that should be explored.

- Reduce to Quit. Unlike the U.S. (where NRT indications generally require the user to stop smoking entirely before using the product), in some countries, indications don't require smokers to quit smoking before they begin using NRT and allow smokers to use NRT to cut down on the number of cigarettes smoked for a period of time as part of their quit attempt. There must, however, be thorough exploration of whether reduced smoking with NRT, in fact, leads to quitting.

- Longer-Term NRT Use. It is clear that, while nicotine is the addictive agent in tobacco products, it is not the one that causes most tobacco-related disease. If longer-term NRT use facilitates abstinence from smoking, indications for such use could prove fruitful and should be seriously examined. Again, the comparison of the risks of longer-term NRT use should be to the risks of continued smoking.

- Dose of Nicotine. Current NRT products do not deliver near the dose of nicotine that tobacco products do. There is evidence that higher dose NRT products may also hold promise.

Several of these approaches would have the effect of making nicotine via NRT more available to consumers. In evaluating their impact, it will be critical to ensure that this results in fewer people smoking, rather than simply helping smokers continue their deadly habit of smoking. A commitment to post-market surveillance will be critical to this evaluation.

In addition to new labeling and indications for existing cessation products, we also strongly encourage FDA to work with responsible companies, genuinely interested in improving public health, to develop a process that will bring new and more innovative and effective NRT and other cessation products to market.

We support the FDA exploring with industry the possibility of the Fast Track process for tobacco cessation products. With tobacco continuing to kill more than 430,000 Americans every year, and smoking declining at a gradual rate, the serious diseases caused by smoking—cancer, heart disease, COPD—represent an extraordinarily devastating and unmet medical need. The Fast Track process should facilitate more engagement between FDA and manufacturers in a process for evaluating innovative products that could bring more innovative products to market, while ensuring that standards for safety and efficacy are not compromised. This, too, will include a commitment from manufacturers to conduct post-market surveillance to ensure the desired outcomes are met. Post-market surveillance is not, however, a substitute for strong clinical evidence; it is a complement.

With its expansive authority over tobacco and nicotine products, the FDA has a unique opportunity and responsibility to protect and promote public health. It is critical that the two Centers—CTP and CEDR—respond proactively and in a coordinated manner to reduce the death and disease from tobacco use that continues to devastate public health in the U.S. By working to reduce the addictive power of tobacco products and working cooperatively with responsible manufacturers to bring more effective smoking cessation interventions to market, FDA can make a huge contribution to reducing death and disease from tobacco use.

Sincerely,

Daniel E. McGoldrick
Vice President, Research