February 3, 2016

Mr. Mitchell Zeller
Director, Center for Tobacco Products
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, Maryland 20993

Dear Director Zeller:

As you have recognized, product standards limiting the allowable levels of certain constituents in tobacco or tobacco smoke can have a profound impact on public health. You also have indicated that the Center for Tobacco Products (CTP) is exploring potential product standards in the areas of toxicity, addiction and appeal. As you are aware, the undersigned organizations have submitted to CTP the recommendations of distinguished scientific researchers, Stephen Hecht, Dorothy Hatsukami and Irina Stepanov of the University of Minnesota, calling for product standards requiring the reduction in maximum permissible levels of TSNAs in cigarettes and TSNAs and other substances in smokeless tobacco products.[1] These reports establish that substantial reductions in toxins for cigarettes and smokeless products can clearly be achieved and would be appropriate to the protection of public health. We write now to highlight two recent developments that underscore the importance of reducing TSNA levels in both cigarettes and smokeless products: (1) FDA's own empirical findings in its premarket authorization orders for Swedish snus; and (2) the recent study by Rostron, et al. on toxicant and nicotine exposure among U.S. smokeless tobacco users.

FDA's Premarket Authorization Orders for Swedish Snus

First, we note FDA's November 10, 2015 issuance of its first orders authorizing the marketing of new tobacco products through the premarket tobacco application pathway. That order authorized the marketing of eight Swedish Match North America, Inc. snus smokeless tobacco products. As noted by FDA in its news release announcing the orders, these orders do

[1] Letter to Mitchell Zeller from Campaign for Tobacco-Free Kids, ACS CAN, American Heart Association, American Lung Association and Legacy (now Truth Initiative), November 21, 2014. *See also* Letter to Mitchell Zeller from Campaign for Tobacco-Free Kids, ACS CAN, American Heart Association, American Lung Association and Legacy (now Truth Initiative), February 4, 2015, transmitting Hatsukami, DC, Stepanov I, Hecht SS. Evidence Supporting Product Standards for Carcinogens in Smokeless Tobacco Products. DOI:10.1158/1940-6207. CAPR-14-0250 (published online first December 18, 2014).

not authorize Swedish Match to market its snus products with modified risk claims. The November 10 premarket orders thus do not resolve the issues raised by Swedish Match's pending modified risk application, which requires an assessment by FDA of the population-wide effects of proposed changes in the existing statutory health warnings as applied to specific Swedish snus products.

FDA's Technical Review supporting the November 10 orders, however, makes several findings that directly support a product standard that would limit TSNAs in smokeless tobacco products. FDA found that the Swedish snus products under review contained significantly lower levels of NNN and NNK, two of the most carcinogenic constituents in tobacco products. Specifically, FDA found that the proposed Swedish snus products contain "significantly lower levels of NNN and NNK compared to over 97% of the ST [smokeless tobacco] products currently on the U.S. market."[2] FDA then quantified the reduction in cancer risk from the lower levels of NNN alone:

> Assuming persons who would have used other US ST products use these product[s] instead, an individual using these products with reduced NNN levels could decrease the excess cancer risk by 90% compared to use of moist snuff (market share: 82%), 67% compared to use of chewing tobacco (market share: 15%), 38% compared to use of United States (US)-style snus, and 92% compared to use of dry snuff.[3]

FDA also found levels of other harmful and potentially harmful constituents (HPHC) in the subject Swedish snus products are similar to or lower than levels in smokeless tobacco products currently on the U.S. market and that, when used exclusively instead of combusted tobacco products, the Swedish snus products offer lower risk of developing respiratory diseases and cancers than smokers.[4]

Thus, although the November 10 orders do not directly address the need for a product standard, the findings supporting the orders establish that (1) reduction in the level of NNN in smokeless tobacco products would substantially reduce the risk of cancer to users of smokeless tobacco products; and (2) it is feasible to produce smokeless tobacco products that would substantially reduce this risk. These findings support the conclusion that a product standard limiting the levels of these carcinogens in all smokeless tobacco products would substantially reduce the risk of disease to users of smokeless tobacco.

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[2] Food and Drug Administration, Center for Tobacco Products, *Premarket Tobacco Application (PMTA) Technical Project Lead (TPL) Review for PM0000010-PM0000017* (TPL Review), at 6.
[3] TPL Review, at 6. FDA added that "[e]ven further reductions in excess cancer risk could occur with the corresponding reductions in NNK," although it added that a quantitative contribution to the reduction in risk could not be determined at this time due to the absence of a NNK cancer slope factor. TPL Review at 6.
[4] TPL Review at 6-7.

Recent Study of Toxicant and Nicotine Exposure among U.S. Smokeless Users

A recent study published in the journal *Cancer Epidemiology, Biomarkers & Prevention*, published by the American Association for Cancer Research (copy attached),[5] provides further support for a product standard limiting TSNAs in cigarettes and smokeless tobacco. The study analyzed biomarker concentrations by tobacco use for 38,024 adult participants in the U.S. National Health and Nutrition Examination Survey (NHANES) between 1999 and 2012. The study found not only that exclusive cigarette smokers had far higher concentrations of the tobacco-specific nitrosamine NNAL and cotinine (a biomarker for nicotine) than nontobacco users, but that exclusive smokeless tobacco users had higher concentrations of NNAL and cotinine than cigarette smokers. The high concentrations of tobacco-specific nitrosamines in cigarette smokers and smokeless users provides further support for a product standard limiting these carcinogens in both product categories, which, as the research we previously submitted to FDA demonstrates, is entirely achievable and appropriate for the protection of public health.

There is little doubt that were FDA to act now to reduce the toxicity of cigarettes and smokeless products, countless Americans would be spared debilitating disease and death from tobacco products. We therefore again urge FDA to use its broad authority to issue product standards to make tobacco products less toxic, as well as to make them less addictive and appealing.

Sincerely,

Campaign for Tobacco-Free Kids

Truth Initiative

[5] Brian Rostron, et al., Nicotine and Toxicant Exposure among U.S. Smokeless Tobacco Users: Results from 1999 to 2012 National Health and Nutrition Examination Survey Data, DOI: 10.1158/1055-9965. EPI-15-0376 (published online first November 18, 2015).