

December 5, 2014

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2014-N-1051—Modified Risk Tobacco Product Applications

To Whom It May Concern:

On behalf of our 158,000 members, we are pleased to comment on modified risk tobacco product (MRTP) applications to label smokeless tobacco products substantially less risky to an individual's health than smoking. We offer these comments in response to your Federal Register notice of August 27, 2014 (79 FR 51183).

As you know, the Family Smoking Prevention and Tobacco Control Act gave the Food and Drug Administration unprecedented authority to regulate tobacco products, including the latest generation of products it deems to be made or derived from tobacco and intended for human consumption. These products include, among others, electronic cigarettes, electronic cigarette cartridges, snus, dissolvable tobacco, tobacco gels, and hookah tobacco.

Unfortunately, there is a scarcity of published research on—and certainly no scientific consensus about—the immediate and long-term effects of these new products on oral health. The lack of published literature makes it virtually impossible to justify claims that these products are somehow less harmful to the oral cavity than combustible tobacco products, or without other adverse effects.

Preventing oral cancer and other tobacco-related diseases has been a longstanding priority for the ADA. We strongly support developing the published research on the latest generation of tobacco products and the immediate and long-term effects of those products on oral health. In the meantime, we urge you to consult with the National Institute of Dental and Craniofacial Research about the current state of published research in this area.

Thank you for providing us the opportunity to comment. If you have any questions, please contact Mr. Robert J. Burns at 202-789-5176 or burnsr@ada.org.

Sincerely,

/s/

Maxine Feinberg, D.D.S.
President

MF:KTO:rjb

/s/

Kathleen T. O'Loughlin, D.M.D., M.P.H.
Executive Director

This page intentionally left blank.

Comments from the American Dental Association’s Council on Scientific Affairs on a Manufacturer’s Application to Reduce the FDA Warning Label for Snus Smokeless Tobacco Products

The ADA Council on Scientific Affairs appointed a group of experts to evaluate a manufacturer’s application for a proposed reduction of the FDA warning label for snus smokeless tobacco products, and to report findings. The following report summarizes these findings, which the Council has adopted.

Background: In 2014, the FDA was contacted by a manufacturer of snus smokeless tobacco with a request to reduce the warning label on packages of snus tobacco marketed in the United States. The company’s rationale for the requested reduction in warning is that the rates of oral cancer and pharyngeal cancer in Sweden, where snus use is prevalent, have reportedly not been elevated. The company also suggested that there is little evidence, based on findings in Sweden, to support the FDA’s current warning label related to the adverse effects of snus on the dental and periodontal health of individuals.

In fall 2014, the ADA Council on Scientific Affairs appointed a group of experts to review the manufacturer’s claims pertaining specifically to oral health, focusing primarily on the proposed claim that snus does not represent a risk for oral disease in the United States population.

The expert panel also considered three primary questions:

1. What is the peer-reviewed published evidence that usage of snus smokeless tobacco products is an important risk factor for squamous cell carcinoma in the oral cavity?
2. What is the peer-reviewed published evidence that usage of snus smokeless tobacco is not an important risk factor associated with periodontal disease and tooth loss?
3. What is the peer-reviewed published evidence that usage of snus smokeless tobacco is not a safe alternative to cigarettes, is no more risky than not using tobacco products, and whether substitution of smokeless tobacco for cigarettes reduces the risk of adverse health effects caused by cigarettes?

Findings: The Council is concerned about the potential risk of increased tobacco fermentation of snus and smokeless tobaccos that may occur in warm southern climates, since exposure to heat has been shown to increase nitrosamines and other carcinogenic agents. While the company cited data from Sweden^{1,2} that suggests the use of snus does not materially increase the risk for oral cancer and other oral diseases, there is minimal, if any, data for the United States that demonstrates that the use of snus products is safe and does not represent possible harm. There is also minimal, if any, data on the effect of snus smokeless tobacco on periodontal disease and tooth loss.

The population of Sweden is relatively homogeneous and significantly different in many characteristics than the population of the United States, which is quite heterogeneous with great variation in social, economic, and educational status. Risk for oral cancer, periodontal disease, and tooth loss in the presence of snus may be related to a host of cofactors present in the United States, but either are not present in Sweden or, if present, are there to a lesser degree. Overall, it is inappropriate to assume that

the patterns of oral disease or lack of oral disease associated with snus are the same in the United States as has been reported in Sweden.

The Council is also concerned regarding whether or not reducing the FDA warning might apply to all forms of smokeless tobacco, including traditional chewing tobacco. Previous studies^{3,4} have shown that the use of smokeless tobacco products made in the United States, as used in some geographic areas of the country, is associated with increased risk of oral soft tissue changes, including premalignant changes of the oral mucosa. The Council also notes that use of smokeless tobacco has been associated with increased risk of cardiovascular disease⁵ and pancreatic cancer.⁶

The Council also questions whether relaxing the warning on snus and other smokeless tobacco products may result in those products acting as a gateway process, leading to increased use of cigarettes.⁷ With respect to the core question of whether there is evidence that snus use in the United States does not represent a risk to individual health and an elevated risk for cancer incidence, the Council concluded that there is no body of scientific evidence in U.S. populations demonstrating that the use of snus is safe.

The Council also concluded that there is no body of data in the U.S. population finding that use of snus is safe and not a risk factor for periodontal disease or tooth loss. In addition, there is no data from the U.S. population to support the claim that smokeless tobacco, and specifically snus, is a safe alternative to cigarettes. Overall, previous research has demonstrated that smokeless tobacco can serve as a gateway to initiate use of cigarettes,⁷ and heavy marketing of smokeless tobacco may promote dual usage of cigarettes and smokeless tobacco,⁸ countering the argument that snus use will reduce smoking.

Summary and Recommendation: Based upon these unresolved issues, the ADA Council on Scientific Affairs opposes any lessening of the warning labels on smokeless tobaccos, including snus products, until definitive studies in the U.S. population demonstrate that long-term use of these products does not materially increase risk for oral disease, including tooth loss, periodontal disease, and other adverse mucosal changes (e.g., oral cancer or premalignant changes). The Council further recommends that no change in product labeling occur in the absence of any peer-reviewed studies demonstrating that use of smokeless tobacco is not a gateway to the initiation of smoking in the U.S. population.

Acknowledgement: The Council would like to acknowledge the following individuals for their valuable input with this report: Dr. Edmond Truelove, professor of oral medicine, University of Washington, and immediate-past chair, ADA Council of Scientific Affairs; Dr. Mark Lingen, professor of pathology, University of Chicago; Dr. Thomas Payne, professor of otolaryngology and communicative sciences, University of Mississippi; and Dr. Dorothy Hatuskami, professor of psychiatry, and associate director, Masonic Cancer Center, University of Minnesota.

References

1. Schildt EB, Eriksson M, Hardell L, Magnuson A. Oral snuff, smoking habits and alcohol consumption in relation to oral cancer in a Swedish case-control study. *Int J Cancer* 1998 Jul 29;77(3):341-6.
2. Lewin F, Norell SE, Johansson H, Gustavsson P, Wennerberg J, Biörklund A, Rutqvist LE. Smoking tobacco, oral snuff, and alcohol in the etiology of squamous cell carcinoma of the head and neck: a population-based case-referent study in Sweden. *Cancer* 1998 Apr 1;82(7):1367-75.
3. Tomar SL, Winn DM, Swango PA, Giovino GA, Kleinman DV. Oral mucosal smokeless tobacco lesions among adolescents in the United States. *J Dent Res* 1997 Jun;76(6):1277-86.
4. Wray A, McGuirt WF. Smokeless tobacco usage associated with oral carcinoma incidence, treatment, outcome. *Arch Otolaryngol Head Neck Surg* 1993;119(9):929-933.
5. Bollinder G, Alfredsson L, Englund A, de Faire U. Smokeless tobacco use and increased cardiovascular mortality among Swedish construction workers. *Am J Public Health* 1994 March; 84(3): 399–404.
6. Luo J, Ye W, Zendejdel K, Adami J, Adami HO, Boffetta P, Nyrén O. Oral use of Swedish moist snuff (snus) and risk for cancer of the mouth, lung, and pancreas in male construction workers: a retrospective cohort study. *Lancet* 2007; 369: 2015–20.
7. Haddock CK, Weg MV, DeBon M, Klesges RC, Talcott GW, Lando H, Peterson A. Evidence that smokeless tobacco use is a gateway for smoking initiation in young adult males. *Prev Med* 2001 Mar;32(3):262-7.
8. Carpenter CM, Connolly GN, Ayo-Yusuf OA, Wayne GF. Developing smokeless tobacco products for smokers: an examination of tobacco industry documents. *Tob Control* 2009 Feb;18(1):54-9. doi: 10.1136/tc.2008.026583. Epub 2008 Oct 23.