

February 15, 2018

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

Re: FDA's Approach to Evaluating Nicotine Replacement Therapies; Public Hearing; Request for Comments (Docket No. FDA-2017-N-6529), 82 Fed. Reg. 56759 (November 30, 2017)

Dear Sir or Madam:

The Consumer Healthcare Products Association (CHPA) welcomes the opportunity to comment on the above captioned request for comments on Nicotine Replacement Therapies (NRT). CHPA, founded in 1881, is the national trade association representing manufacturers of over-the-counter (OTC) or nonprescription medicines and dietary supplements in the United States. A number of our member companies hold new drug applications or abbreviated new drug applications for NRT. As such, we have an interest in the subject matter of FDA's notice.

Our comments cover four areas:

1. General themes on helping people quit smoking and stop tobacco use;
2. An FDA process recommendation;
3. FDA's Question 2: Additional indications or regimens; and
4. FDA's Question 3: Data to demonstrate health benefits of reduction in consumptions of combustible tobacco.

1. General themes on helping people quit smoking and stop tobacco use.

The very fact FDA is holding this hearing is acknowledgement of the power of access: For the past 20 years, having products to stop smoking at least as accessible as those that create nicotine addiction has demonstrated a public health gain. For instance, NRT OTC availability led to over 400,000 more quit attempts over per year, and a 152% increase in NRT-assisted quit attempts the first year following the prescription-to-OTC switch.¹

Quitting smoking provides the greatest personal and public health benefit, but it is evident that smokers or, more broadly, tobacco users, aren't all the same. The path to quit may be shorter or longer. It may be one of abstinence or relapse with multiple attempts. It may be one of limiting

¹Theodore Keeler, et al., *The benefits of switching smoking cessation drugs to over-the-counter status*, 11 Health Economics 389 (January 2002); Saul Shiffman, et al., *Public health benefit of over-the-counter nicotine medications*, 6 Tobacco Control 306 (1997).

exposure, including steps. The fact that an average smoker takes five to seven quit attempts before success only underscores how complex this path can be.

Quitting tobacco and nicotine should remain the objective. Indications that link to reducing harm are positive steps but, as other regulatory authorities such as the UK's Medicines & Healthcare products Regulatory Agency concluded, approving a medicinal product with *only* a “reduce harm” indication is not acceptable.²

It is also important to NRT sponsors for FDA to clearly articulate the agency-wide goal in this area. As we understand it, the agency's goal is two-fold: accelerate the decline in smoking that has occurred among adults, while keeping tobacco products out of children's hands and preventing future generations from becoming addicted in the first place.³ If that is *not* FDA's – reduce smoking while preventing new addictions – we urge FDA to state one.

2. An FDA process recommendation.

FDA has appropriately built a great deal of scientific expertise and capacity within the Center for Tobacco Products. For instance, CTP is developing expertise to understand how specific characteristics of products impact people's attitudes, beliefs, perceptions, and use of these products. CTP scientists are working to understand the effect of different levels of nicotine and other factors on addiction.

That type of expertise is precisely on point for the questions the agency asks in the public hearing notice. FDA, sponsors, and smokers trying to quit would gain from having that expertise utilized directly in drug application review. We recommend FDA explore having a CTP designee be a part of a smoking cessation new drug application review, still under the lead of the Center for Drug Evaluation and Research.

This could be a way to operationalize the agency's commitment to a comprehensive approach to nicotine regulation.

3. FDA's Question 2: Additional indications or regimens.

We agree that additional indications or regimens for OTC NRT products should be explored. A number of examples FDA lists in the hearing notice – craving reduction, relapse, reduce to quit, cessation of non-cigarette tobacco products – are claims tied to the path to quitting.

We stress this path to quitting in combination with thinking about tobacco addiction as a chronic condition for many smokers. Preventing the chronic condition may have already failed for many smokers, so how do we: (a) arrest progression; and (b) reverse it?

² UK Medicines & Healthcare products Regulatory Agency, *Licensing procedure for electronic cigarettes and other nicotine-containing products (NCPs) as medicines*, at 14 (February 2017).

³See remarks by Scott Gottlieb, MD, Commissioner of Food and Drugs, *New Strategies for Tobacco Policy and Therapeutic Nicotine Replacement*, presentation to Duke-Margolis Center for Health Policy, Dec. 12, 2017, at <https://www.fda.gov/newsevents/speeches/ucm588661.htm>.

First, arresting progression: Where logic and literature support a claim that leads to less smoking for those on an attempted quitting path, sponsors should be able to submit stream-lined data packages for these supplemental claims.

In the agency's premarket tobacco product applications for electronic nicotine delivery systems draft guidance, FDA notes, in some cases "it may be possible to support a marketing order for an ENDS product without conducting new nonclinical or clinical studies. For example, if there is an established body of evidence regarding the health impact (individual or population of your product or a similar product that can be adequately bridged to your product, such as data from the published literature or government-sponsored data bases, these data may be sufficient"⁴ The draft guidance goes on to discuss alternatives to randomized controlled clinical trials, including non-concurrent controls or observational studies.⁵ We think a similar approach can be extended to OTC NRT.

Post-approval epidemiologic data that might or might not be product specific, or small scale post-approval studies can further support such claims.

Second, reversing the condition of tobacco addiction: Remembering quitting is the end goal, are we on that path with supplemental claims? A published UK survey-based study found two claims on a potential path to quitting -- smoking reduction or temporary abstinence with nicotine replacement therapy – *were* in fact predictive of quit attempts and abstinence six months later.

We acknowledge such an approach is not without risks, which must be monitored and in turn addressed. Inducing nicotine use by a group that would otherwise be less likely to smoke is an obvious risk if claims short of quitting are too attractive.

One pre-approval means to mitigate risks is to continue to urge NRT sponsors to conduct label comprehension studies on claims.

If FDA pursues a path of literature and epidemiologic data that may not be product specific, we would expect FDA to continue to require a full quality module, and a full safety review, including inactive components in an OTC NRT product. In the case of a supplemental claim, this work would've already been done on the initial new drug application.

These suggestions are all entirely consistent with Dr. Gottlieb's call for improvements in technology of nicotine replacement products, and the fact that "these products have tremendous potential to save lives by empowering people to quit smoking, even if they don't want to cut themselves off immediately and entirely from nicotine."⁶

⁴ FDA, *Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems*, draft guidance, at 44 (May 2016).

⁵ *Id.*

⁶ Gottlieb, *supra*.

These suggestions also apply to the use of more than one format of NRT in combination, such as a patch and a lozenge or gum.

4. FDA’s Question 3: Data to demonstrate public health benefits of reduction in consumption of combustible tobacco products.

A number of the speakers at FDA’s January 26 public hearing provided perspectives on this question, which we would encourage the agency to examine closely.

In brief, we would draw FDA’s attention to three specific study findings:

First, researchers in South Korea concluded there was a risk reduction in reduced smoking, but the size of risk reduction was disproportionately smaller than that expected from the reduced amount of cigarette consumption. The authors went on to suggest cessation remain the cornerstone of preventing smoking-related cancers, but smoking reduction could be considered as a strategy to supplement smoking cessation.⁷

Second, snus studies in Sweden suggest reduced risks of lung cancer or chronic obstructive pulmonary disease, but with continued risks and potential greater risk of other types of cancer. One qualifier to note is that these studies speak to snus versus smoking, as opposed to dual use.⁸

Third, the UK’s National Institute for Health and Care Excellence notes there are no circumstances where it is safer to smoke than to use medicinal nicotine and there is reason to believe that lifetime use of licensed nicotine-containing products will be considerably less harmful than smoking.⁹

We thank you for the opportunity to present at the public hearing and to provide these comments. CHPA members want to do their part in making tobacco-related death and disease part of America’s past.

Respectfully submitted,

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⁷ Yun-Mi Song, et al., *Reduction and Cessation of Cigarette Smoking and Risk of Cancer: A Cohort Study of Korean Men*, 26 *Journal of Clinical Oncology* 5101 (November 2008).

⁸ P.N. Lee, *Summary of the epidemiological evidence relating snus to health*, 59 *Regulatory Toxicology and Pharmacology* 197 (2011); and Karl Fagerstrom, et al., *Tobacco harm reduction: the need for new products that can compete with cigarettes*, 39 *Addictive Behaviors* 507 (2014).

⁹ UK National Institute for Health and Care Excellence, *Smoking: harm reduction*, Public health guideline (PH45), June 2013, July 2013 update.